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MIRKIN

ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND  
RELATED MATTERS.

Hearing held  
8th floor  
180 Dundas Street West  
Toronto, Ontario

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The Honourable Mr. Justice S.G.M. Grange

Commissioner

P.S.A. Lamek, Q.C.

Counsel

E.A. Cronk

Associate Counsel

Thomas Millar

Administrator

Roland

Transcript of evidence  
for

January 11, 1984

Chow

VOLUME 88

McIntyre

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ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
DEATHS AT THE HOSPITAL FOR SICK CHILDREN  
AND RELATED MATTERS.


Hearing held on the 8th Floor,  
180 Dundas Street West, Toronto,  
Ontario, on Wednesday, the 11th  
day of January 1984.

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner  
THOMAS MILLAR - Administrator  
MURRAY R. ELLIOT - Registrar

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	Nurse
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	Nurse
J.A. OLAH	Counsel for Janet Brownless -
	R.N.A.

(Cont'd.)...



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Mr. & Mrs. Gionas, Mr. & Mrs.  
Inwood, Mr. & Mrs. Turner and  
Mr. & Mrs. Lutes (parents of  
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W.W. THOMAS Counsel for M. & Mrs. Hines  
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J. SHINEHOFT Counsel for Lorie Pacsai and  
Kevin Garnet (parents of  
deceased child Kevin Pacsai)

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--- on commencing at 10:00 a.m.

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DR. BERNARD L. MIRKIN, Resumed

THE COMMISSIONER: Yes, Mr. Lamek.

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MR. LAMEK: No, Mr. Commissioner,

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I had finished my examination yesterday.

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THE COMMISSIONER: Oh, yes, sorry.

8

Mr. Brown?

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CROSS-EXAMINATION BY MR. BROWN:

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Q. Yes, Doctor, my name is

11

Brown and I am one of the lawyers that acts for

12

Registered Nurse Susan Nelles. There are only two

13

areas that I would like to ask you questions on

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today. The first is regarding your testimony

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yesterday in respect to the Baby Velasquez. Am I

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correct, Doctor, that it was one of your conclusions

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yesterday that you would be very surprised if the

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drug naloxone had poisoned the child?

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A. That is correct.

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Q. I believe you were also

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asked about your opinion as to the involvement of

22

digoxin in the death of the child and if I recall

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your opinion was that you thought the possibility

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of that happening was not very great.

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A. That is correct.

Q. Mr. Lamek yesterday reviewed





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with you in some detail the terminal events surrounding the death of the child and indicated to you that the child appeared . . . afebrile slightly prior to his demise. Do you recall that?

A. I do.

Q. He then indicated that the child was demonstrating some somnolence. Am I correct in saying that you were of the opinion that this manifestation was more consistent with the codeine administered to the child?

A. That is correct.

Q. If I also recall you said that digoxin if given in a large quantity could possibly induce shock which might manifest somnolence but in view of the blood pressure that this child demonstrated in his left arm you thought that this was unlikely and there was no evidence of that?

A. Yes.

Q. Also, the pupils of the child were constricted and if I recall you thought that that was due to the drug codeine administered to the child?

A. The drug...?

Q. Codeine which had been





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administered to the child.

A. Yes.

Q. I believe Mr. Lamek asked you to assume that digoxin had been administered. Am I correct in saying that one of the factors you thought militated against digoxin was a finding that the liver edge in the child was sharp, it was 2 centimetres below the costal margin. If the child had been on digoxin you would have expected some manifestations of congestive heart failure and this was not indicative of that condition?

A. Well, may I correct that interpretation slightly?

Q. Certainly.

A. I think I did indicate that the fact that the liver was not larger, as evidenced by a size that would allow it to be felt or palpated more than 2 centimetres below the right costal margin. The absence of that in my opinion suggested that the patient was not in a shocklike state, was not in congestive heart failure and that had a large overdose or an overdose sufficient of digoxin, sufficient to cause an effect on the heart been given, I would have anticipated impairment of cardiac function by the drug





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with the appearance of drug-induced congestive failure.

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I hope that is not too confusing.

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Because, as you will recall, digoxin itself is used to treat endogenously occurring congestive heart failure. When the heart is not pumping effectively it needs digitalis or digoxin to improve it.

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What I am trying to imply is that with a large amount of digoxin and once the toxic effects are manifest, you can throw the heart, a normal heart into dysfunction and produce symptoms similar to heart failure that would occur in a sick heart. So, that was the basis, one of the bases for my opinion.

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Q. Well, had digoxin been administered in a large dose and had sufficient time elapsed to allow the manifestation of toxic effects, would one necessarily expect to find a symptom of congestive heart failure manifesting itself in the liver?

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A. I think one might. It is not an absolute assurance that it would be there but I think if heart failure had occurred as a consequence of that theoretical event, then I think





1  
2 the liver in this patient might have been down. I  
3 think it is a reasonable conclusion.

4 Q. I believe there was one  
5 other terminal symptom put to you that at some  
6 point the child manifested bradycardia. Am I  
7 correct in saying that it was your opinion that  
8 this was really the only symptom which would be  
9 indicative or consistent with digoxin intoxication?

10 A. Yes, at least of those  
11 that were described in the chart.

12 Q. That is correct. Mr. Lamek  
13 asked you to assume during the course of your testi-  
14 mony yesterday afternoon that in addition to the  
15 drug codeine being administered to the child a large  
16 dose of digoxin was also administered to the child.  
17 Am I correct in saying it was your opinion that  
18 given that assumption and the subsequent administra-  
19 tion of naloxone, under those conditions the  
20 naloxone would still antagonize or reverse the  
21 effects of codeine?

22 A. Yes, that was a correct  
23 interpretation.

24 Q. And if I also recall you  
25 put one caveat on that, that conceivably the  
administration of such a large dose of digoxin might





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somehow affect the antagonistic effects of naloxone and it might not reverse the symptoms attributed to the codeine. Is that also accurate?

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A. Yes. I think though that we probably should be more specific with which symptoms we are talking about. When you say symptoms that in a sense is a generic statement.

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Q. Well, the child, if I might interrupt, was demonstrating some somnolence. There was also a constriction of the pupils. The naloxone was administered, the child revived to some extent and the pupils dilated to some extent. Those were the two symptoms that I was referring to.

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A. Now you are being specific and you are correct.

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Q. Okay. Also given that assumption that Mr. Lamek put to you, was it your opinion that the posturing which was observed after the second dose of naloxone was given more probably was a result of an effect on the central nervous system?

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A. Of which drug?

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Q. The second administration of naloxone.

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A. Correct.





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Q. The posturing which followed the second administration of the drug naloxone.

A. Yes.

Q. Was it your opinion that the posturing most likely was caused by some effect on the central nervous system rather than the hypothetical administration of digoxin which Mr. Lamek asked you to assume?

A. By some effect on the central nervous system induced by an unknown factor. Now you are not inferring that the effect on the central nervous system that we saw was caused by naloxone are you in this question?

Q. Well, I was unclear as to exactly what you meant. Perhaps you could explain that to me. What is your opinion as to the cause of the posturing?

A. I don't know the cause of it. I would not believe that it was due to the naloxone.

Q. Is it possible that it could have been due to digoxin assuming the drug was there?

A. That would have been an unusual manifestation of digoxin intoxication but





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I think you asked is it possible and I think the possibility does exist but I would say though that it is put in the slim possibility that this is a common expression of the toxic effects of digitalis.

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Q. In your opinion is there any other apparent cause for this posturing?

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A. None that I could discern from the patient's chart other than the possibility that this represents an agonal effect in the terminal events of this patient's life.

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Q. If I recall, when Mr. Lamek put the assumption to you about the administration of digoxin, you indicated that if the bradycardia which had been observed in this child had been a manifestation of digoxin toxicity, that you would not expect the heart rate in the child to have increased to a rate of 130/140 as it did after the administration of naloxone. Is that an accurate recollection on my part?

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A. That is a precise statement.

Q. And as a result of that am I correct in saying that it was your opinion that the increase in the heart rate suggested that the bradycardia was not due to digoxin intoxication?

A. That is correct.





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O. And then the fourth opinion which I believe you reached, given the assumptions which Mr. Lamek put to you, were that after the second dose of naloxone was administered it was observed that a very short period of time thereafter the activity of the heart ceased, the heart stopped. While you were not prepared to eliminate the possibility of a digoxin overdose you would not expect it to manifest itself so rapidly. Am I accurate in recalling that observation on your part?

A. I think that the last part, if I did say that then I was a little bit inaccurate. I was really trying to get at a clarification, how one could postulate giving digoxin in that interval between the last dose of naloxone and the death of the patient. There was a temporal association there that I wanted to clear up with you. I think you just stated that. I stated yesterday that the effect of digoxin might not be manifest in such a short time. Is that exactly what you have just told me?

Q. Perhaps I can clarify it this way. I was assuming that the digoxin in the hypothetical had been administered before the naloxone.

A. The second or first dose?

Q. The first dose of naloxone.





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A. That would be six hours prior  
to the demise of the patient, as I understood it.

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Q. Some time within a period  
of six hours prior to the demise?

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A. Yes.

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Q. It was on the basis of that  
understanding of mine that I thought you were  
suggesting that when a second dose of naloxone was  
administered, given that digoxin might already be  
present in the child, one would not expect to see  
a cessation of the heart activity so quickly?

12

A. No.

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Q. Am I incorrect?

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A. I think you are, in the  
conclusion. The sequence of events in that scenario,  
as I recall it, in those terms, if one postulates  
that the digoxin was given at six hours or about the  
time of the first naloxone dose then certainly,  
whether the drug was given orally, intravenously  
or inter-muscularly, this effect would have been  
manifest at the time, six hours later. Its effect  
probably would have been manifest much earlier  
depending on the routing. You have heard this from  
other experts, with the intravenous route almost  
immediately, within 15 or 20 minutes; with the oral





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B3 2 route, the peak absorption would be within an hour  
3 and probably the effect would have been manifest  
4 in two hours at the latest; with inter-muscular,  
5 somewhat shorter than that.

6 So I would have anticipated, were  
7 digoxin administered at around five or six hours  
8 before the demise that we would have had at the  
9 terminal event a profound effect of digoxin manifest.  
10 Based on that reasoning I concluded that the effect  
11 of naloxone in reversing the diminished heart rate  
12 and reversing the miosis, that is narrowed pupils,  
13 those effects were manifest by an action against  
14 the codeine. Had digoxin been present we would  
15 probably have not have gotten such a reversal of  
16 the heart rate because digoxin, as you know, would  
17 have slowed the heart rate. It is my understanding,  
18 current up until this moment, that naloxone will not  
19 exert a meaningful effect against these toxic actions  
20 of digoxin whereas it will against the codeine.  
21 Is that clear?

22 Q . That is clear, but it's not  
23 what I was asking.

24 THE COMMISSIONER: That was my  
25 understanding, too. My understanding of what you  
said yesterday was that you said there should be some





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2 effect of the digoxin if it had been administered.  
3 In many of the ones that you have assumed to be  
4 digoxin intoxication you have seen an immediate -  
5 not an immediate effect upon the dose but a very  
6 sudden effect, after the child has been stable.  
7 What is concerning me about the Velasquez case  
8 is that it is complicated by the codeine and the  
9 naloxone. If we just assume that there was some  
10 administration of digoxin at some point, we don't  
11 know when it was, and its effect takes place  
12 coincidentally with the last administration of  
13 naloxone, is that an impossibility? Naloxone could  
14 do all its work in the first application quite  
15 reasonably because the digoxin had not taken any  
16 effect at all and then the digoxin takes its effect,  
17 as it happened, approximately the same time as the  
18 second dosage of naloxone. Let us forget for the  
19 moment about the symptoms not being precisely what  
20 you would expect with digoxin poisoning, but on the  
21 time question is there any reason why that could  
22 not have happened? We have codeine, naloxone,  
23 a second naloxone and somewhere, we don't know when,  
24 the administration of this overdose of digoxin  
25 and it takes effect just about the time that the  
second naloxone dose is administered.





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THE WITNESS: The argument against that conclusion --

THE COMMISSIONER: One of the arguments is that the symptom are not correct. We have been through that. I'm just talking about the timing problem.

THE WITNESS: The symptoms are almost the least important to my mind right now. The most important evidence or information that mitigates against that - mitigates? Militates against that.

THE COMMISSIONER: Militates - however, you are in good company because almost every counsel here confuses the two words, but I am delighted to know that you are least worried about it.

THE WITNESS: Not worried, concerned. Well, the most important information that I can offer on this, or the point that I can raise on this, is that the naloxone reversed the decreased heart rate. It reversed it.

THE COMMISSIONER: You will have to help me with that because what I was putting to you was that the slow heart rate, the bradycardia, was not the result of anything but codeine - was not the result of digoxin.





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THE WITNESS: Okay, let us take that possibility that the effect we are seeing there right at the time the last dose of naloxone was given was due strictly to the codeine. We gave the naloxone and we reversed some of the effects of the codeine.

THE COMMISSIONER: On the first dose?

THE WITNESS: Also on the second.

THE COMMISSIONER: I thought almost immediately after the second one, the heart rate stopped.

THE WITNESS: It was right after the second.

THE COMMISSIONER: So it was the first dose of naloxone that apparently did the job.

THE WITNESS: Okay. Then the inference is that the reason the second dose is ineffective is that we are having manifest an expression of digitalis intoxication. One could postulate that, I think one could, and I would have to accept that reasoning.

THE COMMISSIONER: All right.

THE WITNESS: It is a possibility. Do you think I could have that chart?

THE COMMISSIONER: Certainly.

THE WITNESS: I want to check through





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something.

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MR. BROWN: Q. Doctor, assuming the presence of digoxin in toxic quantities, before the administration of naloxone, is the fact that after the second administration of naloxone there was almost an immediate cessation of heart activity and indication that, in your mind, digoxin in toxic dose was not present in the child?

A. Do you mind if I repeat that question so I understand it. Given the fact that the heart stopped after the second dose of naloxone --

Q. Shortly after the administration of the second dose.

A. Yes. Is it my opinion that a toxic dose of digoxin was not present?

Q. Yes.

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THE COMMISSIONER: I am having trouble  
with that question, too, I don't know quite what  
you mean.

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Q. Is there a misunderstanding;  
it was my understanding, obviously mistaken,  
of your testimony yesterday that the fact that  
there was such a significant temporal relationship  
between the administration of the second dose of  
naloxone and then the cessation of heart activity  
shortly thereafter, that that observation would  
suggest digoxin in toxic quantity was not present  
in the child.

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A. Why would --

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Q. I don't know why. If that  
is not what you said, if that is not your opinion,  
please correct me on that.

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A. I think if it did come out  
that way, it was --

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THE COMMISSIONER: If it is any  
comfort to you, you never said anything of the sort.  
What he did say was he doesn't think anything of the  
naloxone theory, but he also thinks one out of ten  
on the digoxin theory, too, did I not get this  
correct?

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THE WITNESS: Yes, I thought the





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likelihood of digoxin intoxication, very slim. Okay?

Q. Yes, we established that a long time ago.

A. But I would not -- excuse me --

THE COMMISSIONER: No, it's all right, carry on.

Q. I just want to clear up that misunderstanding on my part, then, of the temporal relationship between the administration of the second dose of naloxone and the cessation of heart activity was not a factor weighing in your opinion that the possibility of digoxin toxicity was slim? Well, that you did not, that the temporal relationship between the administration of the second dose of naloxone and the sudden cessation of heart activity was not a significant factor in your mind?

A. Well, it was a significant factor, I didn't understand the etiology for this cessation of this patient's heart, because, okay, I don't understand it.

Q. Did that in your mind preclude the possibility of the presence of digoxin in toxic dose?

A. No, it didn't preclude it.

Q. Then it was a misunderstanding





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then on my part.

A. Okay.

Q. We are clear on that point.

A. We are clear, good.

Q. Yesterday, at the end of your testimony, I gave to you two articles which I asked you to read if possible over the evening, were you able to read those articles?

A. Yes.

Q. If I might then put them to you.

THE COMMISSIONER: The exhibit numbers, have they been exhibited?

MR. BROWN: No, they have not been presented as exhibits.

Q. The first is an abstract from the Annual Meeting of the Canadian Cardio-Vascular Society held October 19th to the 22nd, 1983 in Toronto. There is an abstract by Dr. Rabkin, R-a-b-k-i-n, and a Dr. Roob, R-o-o-b, and I would ask that that be marked as the next exhibit.

THE COMMISSIONER: Exhibit 315.

---EXHIBIT NO. 315: Abstract from the Annual Meeting of the Canadian Cardiovascular Society, October 19-22, 1983 by Dr. Rabkin and Dr. Roob.

MR. BROWN: The next one is an





1  
2 article entitled: "Bidirectional Effect of  
3 Naloxone on Emotionally Conditioned Digitalis  
4 Toxicity" by Dr. Natelson, appearing in Psychosomatic  
5 Medicine, Vol. 44, No. 4 (September, 1982).

6 THE COMMISSIONER: Exhibit 316.

7 ---EXHIBIT 316: Bidirectional Effect of Naloxone on  
8 Emotionally Conditioned Digitalis  
9 Toxicity, excerpt from Psychosomatic  
10 Medicine, Vol. 44, No. 4 (September,  
11 1982).

12 Q. Doctor, can I first turn your  
13 attention to the abstract from the proceedings of the  
14 Canadian Cardiovascular Society, the work by  
15 Rabkin. Am I correct in reading that abstract that  
16 Dr. Rabkin was attempting to prove a hypothesis  
17 to the effect that something called endogenous opioids  
18 antagonize digitalis arrhythmias, if that was the  
19 purpose of the study to establish that hypothesis?

20 A. That's correct.

21 Q. And that in order to establish  
22 that hypothesis he constructed an experiment, the  
23 experiment consisting of using an animal, I think a  
24 guinea pig. These animals were anesthetized with  
25 a drug called Pentathol After they were anesthetized  
they were then digitalized with a high dose of  
digoxin, I believe 100 micrograms per kilogram.

A. Ouabain.





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Q. I believe in this study it was digoxin, I think ouabain was the other study.

A. You are right.

Q. After the administration of digoxin the animals were separated into two groups and to one group naloxone was administered in the dose of two milligrams per kilogram; and in the second group the diluent was administered, and I take that to mean that substance not containing naloxone was administered to the second group. Is that your understanding of the drugs that were administered to these animals in the experiment?

A. Yes, that is correct.

Q. After then the administration of the naloxone the doctors observed the effects on the guinea pigs and that there were arrhythmias present in both groups because of the administration of digoxin, is that correct?

A. That's correct.

Q. In the group which had received the naloxone they noticed a manifestation of a high degree of AV block, followed by ventricular tachycardia or fibrillation, and were those the manifestations of heart activity that they noted in the group





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of animals administered naloxone?

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A. Yes, but go on.

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Q. In addition to noting that they also noted a temporal phenomenon, if I might call it that, inasmuch as the group of digitalized animals who had been administered naloxone had a survival rate of approximately 7 minutes, and the doctors observed that this survival rate was significantly shorter than the survival rate of about 17 minutes in the group that had not been administered naloxone. Is that an accurate summary of the observations in that experiment?

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A. Yes, with one major omission. I think you should indicate that the controlled animals also had cardiac arrhythmias.

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Q. Yes, I am sorry, both groups were first administered digoxin.

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A. So I think it is important to emphasize that not only did the animals receiving the naloxone and the digoxin develop arrhythmias but the group receiving digoxin alone developed the same arrhythmias.

Q. Indeed both groups were administered large doses of digoxin, were they not?

A. That is correct.





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Q. And it was only after the manifestation of cardiac arrhythmias in both groups that they were separated into two different groups, I believe the sentence is:

"After the development of arrhythmias the animals were randomized into two groups."

A. Yes, that is correct.

Q. Given the administration of digoxin of that quantity one would expect the guinea pigs to die at some time. One of the temporal phenomena which they observed, however, was that, was it not, that the animals administered naloxone died more rapidly than those not administered naloxone, is that accurate?

A. Yes, that is accurate.

Q. Now, Doctor, the reason I put this abstract to you was because of the sequence of the administration of the drug that there was an anesthetic administered to the group; that the group was subsequently administered a very large dose of digoxin. After that had been administered and the arrhythmias were manifest they were then separated into two different groups, one group got naloxone and one group did not. On the basis of the arrhythmias





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shown by the guinea pigs in the group that received  
naloxone, that is the high degree of AV block  
followed by ventricular tachycardia or fibrillation,  
can one on the basis of this experiment say that the  
administration of naloxone in a highly digitalized  
animal could possibly have the effect of increasing  
the heart rate in that animal?

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A. No, I think everything that you are describing follows but why do you suggest that this would increase the heart rate?

Q. That it would ...?

A. Increase the heart rate.  
Is that what you said?

Q. Well, I am trying to understand what these doctors observed during the course of their experiment.

A. Yes. Well, what they observed was what you described.

Q. I'm sorry, they observed a high heart rate, or a fast heart rate inasmuch as they did have the tachycardia.

THE COMMISSONER: Does that mean a high heart rate?

THE WITNESS: No.

THE COMMISSIONER: A high degree of AV blocks was most frequent.

THE WITNESS: Yes, I think one of the things that you are perhaps misinterpreting here, if I may suggest, is that there is no suggestion as far as I could discern of an increase in heart rate. You see, if you look in here, read the abstract, we are down eight lines from the bottom, that is, up





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D2 2 eight lines from the bottom, the centre starting:

3 "In contrast naloxone resulted in a  
4 rapid development of fatal  
5 arrhythmias. A high degree of AV  
6 block was most frequent."

7 So, you have there a manifestation  
8 of digitalis intoxication, okay, that is one aspect  
9 of it. This is followed by ventricular tachycardia.  
10 Now, that is a rapid ventricular rate. When you  
11 talk about an increase in the heart rate we are  
12 generally speaking about a synchronized heart rate,  
13 that is, where the atrium, that is the top part of  
14 the heart beats and then the bottom, the ventricular  
15 component beats. In this particular case I would  
16 infer from these data, very scanty data, that they  
17 did not see an increase in heart rate necessarily,  
18 they saw first AV block and as you know from past  
19 testimony that would tend to decrease the ventricular  
20 heart rate. Okay?

21 Q. Yes.

22 A. So, if I were looking at this  
23 I would expect that in the naloxone treated animals  
24 I would have seen a profound fall in the heart rate  
25 as the AV block increased, okay?

26 Q. Yes.





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A. Which was then followed by a speeding up of the ventricular and then to fibrillation. That is the sequence as I interpret it. To go further, I think - well, why don't I listen to what questions you wish to address to me.

Q. Well, given then that the heart rate then - you I take it then are of the opinion then that on the basis of the data present in this that the experiment does not stand for the proposition that the administration of naloxone to a group of highly digitalized animals necessarily increases the heart rate, that is not observed?

A. No. The reason I concluded that is that it says in here a high degree of AV block, okay.

Q. Okay.

A. Now, is that clear?

Q. Oh, yes, that is very clear.

A. Now, that is my interpretation of these data, okay?

Q. Yes.

A. And I can go to the board and confer with it if you like.

Q. No, I understand that. Well then the second point, turning away from the mani-





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festations cardiac activity, the temporal relationship shown between the administration of naloxone and the cessation of heart activity, or the death of these animals, it was observed I believe in this study that those digitalized animals administered naloxone died more rapidly than those not administered naloxone?

A. That is correct.

Q. Okay. Now, in view of this abstract and in view of that temporal relationship, does that in any way alter your opinion as to the possible role of digoxin in the death of baby Velasquez?

A. It doesn't. However, I should add that these are very interesting findings and I think it points out a potential interaction that might have occurred between naloxone and digoxin if it indeed were present in this patient. It is important to add though that in this particular situation extremely large quantities of naloxone were given, probably in the context that was given to the Velasquez baby, the orders of magnitude are, you know, extraordinarily different.

Q. Extremely different.

A. We must bear that in mind.





1  
D5 2 But I think you should really be commended on digging  
3 this up because it is an interesting point.

4 Q. Why in your opinion does it  
5 not change the possibility that digoxin was involved  
6 in the death of the child?

7 A. Well, I think it is  
8 important to recognize that the extrapolation of this  
9 finding to the case we are discussing is monumental.  
10 I don't think that, nor would you I think if you  
11 analyzed this critically, think that would be  
12 possible to take this set of symptoms and say merely  
13 because a set of symptoms occurred in this  
14 experimental model that that is what occurred in  
15 this case under question.

16 Q. So, all we can really say  
17 about this abstract is that in a group of experimental  
18 animals that in one group administered naloxone  
19 they observed a more rapid demise than in the group  
20 not administered naloxone?

21 A. Yes, and I would go one  
22 step further.

23 Q. Yes.

24 A. There is the potential  
25 evidence from this abstract that the high doses of  
naloxone, or the naloxone given in conjunction with





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D62 toxic doses of digoxin potentiate the effects of  
3 digoxin, they enhance the effects, correct?

4 Q. Okay.

5 A. The experiment is a bad  
6 one. It is a very poor experiment. It is not  
7 carried out in any kind of appropriate pharmacologic  
8 context. Now, the abstract admittedly is a very  
9 brief glimpse into what the authors may have done,  
10 so, I don't want to be publicly too negative on  
11 it until I see all the information. But if this  
12 is what they have done then what we need really is  
13 a broader interpretation and examination of the  
14 data to see whether or not the naloxone actually  
15 reduced the amount of digoxin that was necessary  
16 to produce these events. That would be very useful  
17 and I think helpful information. You could perhaps  
18 check with them to see if they have done it.

17 Q. If I could turn you then to  
18 the second article, the one by Dr. Natelson. I  
19 understand that this was a different type of  
20 experiment inasmuch as that the animals which formed  
21 the subject matter of the experiment were not  
22 anesthetized at the beginning of the experiment, is  
23 that correct?

24 A. That is correct.  
25





1 Q. The animals had been divided  
2 into two groups; one group had been subject to  
3 a signal and another group had been subject to a  
4 signal followed by a shock, is that accurate?

5 A. Yes.

6 Q. To these two groups a dose  
7 of naloxone were administered what they term a low  
8 dose and a high dose. After the administration of  
9 those doses of naloxone the drug ouabain was then  
10 administered which I take it is a cardiac-like aside  
similar in sorts to digoxin?

11 A. That is correct.

12 Q. This drug was administered  
13 subsequently, naloxone was administered again to  
14 the two groups, in a low dose and a high dose after  
about 45 minutes, is that correct?

15 A. Yes.

16 Q. And again in this particular  
17 paper the doctors observed certain temporal phenomena?

18 A. Yes.

19 Q. Am I correct in saying that  
20 the temporal phenomena that they observed was that  
21 in the group who had been administered a low dose  
22 of naloxone the time which it took for a signal shock  
23 to precipitate a ventricular arrhythmia was increased  
24 over a group which had not been administered naloxone  
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over a controlled group, is that accurate?

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THE COMMISSIONER: I'm sorry, could  
4 you help me out. I know that was a long sentence.

5

MR. BROWN: I'm sorry. Am I correct  
6 there were three groups of these animals. You have  
7 read the article, have you not?

7

A. I told you yes earlier.

8

Q. Yes, okay.

9

A. The statement you just made  
10 is perfectly accurate and correct. It is a precise  
11 interpretation of what is described in figure 1.

12

THE COMMISSIONER: The trouble is  
13 I didn't quite get that.

13

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THE WITNESS: Okay, why don't you  
14 use figure 1.

15

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THE COMMISSIONER: I didn't quite get  
16 the question. I take it this is supposed to say that  
17 naloxone brings on the toxicity earlier or what?

17

18

MR. BROWN: No. There were three  
18 groups of animals, were there not; one group of  
19 animals was administered I believe a saline solution,  
20 then they were administered digoxin and this was  
21 the control group, is that correct?

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22

A. Correct.

23

Q. In this control group one

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group of the animals was subjected to a signal and they observed the amount of time it took for those animals to develop ventricular arrhythmias, a second group was subjected to a signal and a shock and they observed the length of time it would take for them to manifest ventricular arrhythmias, is that correct?

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A . Correct.

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Q. Simply dealing with this control group to whom they administered the saline. Did they observe that those animals who were administered the signal and the shock develop these ventricular arrhythmias more rapidly than those who were subject to the signal alone, is that correct?

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A . Yes.

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Q. Okay. And that is the control group that we are dealing with. They then had two other groups of animals which they wanted to measure against the control group; one group of animals they gave naloxone in the low dose, they then gave ouabain, and they then subsequently administered naloxone in the low dose, am I correct in that?

23

THE COMMISSIONER: I'm sorry, they

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gave naloxone and then they gave what?

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MR. BROWN: Ouabain, o-u-a-b-a-i-n.

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THE WITNESS: It is pronounced  
wahbain 'w-a-h-b-a-i-n', excuse me. Is it wahbain  
in Canada?

6

7

MR. BROWN: It is a digitalis.

8

THE COMMISSIONER: Oh, that is a  
form of digoxin, is it?

9

10

MR. BROWN: It is a form of digitalis  
I believe.

11

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THE WITNESS: Yes, it is a form of  
digitalis, that is correct.

13

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THE COMMISSIONER: Well then, that  
is easier for me then. Yes, all right, and then  
the third group, I'm sorry.

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MR. BROWN: Well, perhaps if I could  
just deal with the second group.

17

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THE COMMISSIONER: Yes, all right.

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MR. BROWN: Q. With the low dose  
of naloxone group, again, the animals were given  
a signal, they observed the amount of time it would  
take for the ventricular arrhythmia to develop.  
The other group of animals given the signal shock,  
they observed the amount of time it took for the  
arrhythmia to develop. Am I correct in saying that  
what the doctors observed in this experiment is that





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the effect of a low dose of naloxone was to extend the time it took the group of animals subsequent to the signals of shock to manifest their ventricular arrhythmia, is that accurate?

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A. That is accurate.

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Q. So, the administration of the low dose of digoxin and the presence of - I'm sorry, the low dose of naloxone and the presence of ouabain seemed to have the effect of extending the amount of time it took to manifest the ventricular arrhythmia. Is that accurate?

12

A. In the conditioned animal.

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Q. That is correct. Then there was a third group of animals. These animals were given a high dose of naloxone, they were then administered the drug ouabain and they were subsequently administered the drug naloxone in high dose.

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Now, am I correct in saying that in this group they observed that the administration of a high dose of naloxone had the effect of shortening the period of time for the manifestation of these ventricular arrhythmias in the, what did you call it, the signal shock animals, is that accurate?

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A. Yes.

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Q. So what we then see here  
are some different temporal relationships, are they  
not, between the administration of naloxone and  
the administration of a digitalis drug?

A. Concentration-dependent  
effects, you mean?

Q. That is right. That when  
a low dose of naloxone was administered, it tended  
to extend the amount of time for the manifestation  
of the arrhythmia; is that correct?

A. That is correct.

Q. And if a high dose was  
administered it tended to shorten the time for  
the manifestation of the arrhythmia; is that  
accurate?

A. I don't know if the high  
dose was significantly different from the saline  
treated controls, and I want to look -- on Table 1,  
page 399 of your document, we can get that information.  
I cannot tell from this report -- if you look at  
figure 1, Mr. Commissioner, you will see figure 1 -  
this is page 398 now - you see six bars. May I  
go with this? I think it might help a bit.

On the left where the numbers 18  
and 22 are on the bottom, the open bar which is  
described as signal shock, those are animals which





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are conditioned to an electrical stimulus and when you condition them in the presence of ouabain they will develop ventricular arrhythmias at a rate here which is 60 minutes after the administration of the drug. The latency to VT refers to latency, that is the time it takes to develop a ventricular tachycardia or ventricular arrhythmia, so it took 60 minutes for the conditioned or signal shock animal. The control where a signal is given or a light goes on and no stimulus is given to the animal, those animals in the hatched which have the number 22, it took roughly about 78 or 80 minutes for those animals to show an arrhythmia.

Counsel now suggests - or this data really suggests that the low naloxone treated animals in the next column, you see No.9 on the bottom of the open bars, the naloxone is given now in advance of the ouabain - you give the low dose of naloxone -

THE COMMISSIONER: Given before and after as I understood that from Mr. Brown.

THE WITNESS: You are correct, that is actually precise. Where the animal is given the low dose you seem to have a prolongation of the time it takes to develop the arrhythmia where in the controls there is no change. You go to the





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2 next bar, the high naloxone which is the open bars,  
3 No.14 on the bottom and you see that there is a  
4 return to the increased sensitivity.

5 Now, the question that I am asking,  
6 I don't seem to have the data, is whether there is  
7 a significant difference. I think you inferred this,  
8 and I don't believe it is correct from the data, but  
9 I may be wrong, between the saline signal shocked  
10 animal and the high naloxone. Those animals given  
11 high naloxone concentration did not necessarily  
12 rate a shorter time to develop their arrhythmia  
13 than the controlled group because I cannot find in  
14 this data, I will have to look at it again, significant  
15 difference.

16 THE COMMISSIONER: What was the  
17 purpose of the saline solution anyway? What does  
18 that do? How does that help?

19 THE WITNESS: The importance of that  
20 of course is to have a base line response, how  
21 do these animals respond to no treatment alone versus  
22 a treatment.

23 THE COMMISSIONER: What does the  
24 saline do?

25 THE WITNESS: The saline is a salt  
solution and it is essentially a negative control so





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2 that there are animals who are given the ouabain in  
3 the absence of any free treatment other than the  
4 saline.

5 THE COMMISSIONER: To me what you  
6 are saying is to make sense out of the experiment  
7 you would have to have the same kind of animals,  
8 the low and the high, as they have in the saline  
9 solution, but surely that is what they would have  
10 done, would they not have done that?

11 THE WITNESS: No, no, they have done  
12 that. I think the experiment is fine. What I am  
13 questioning is whether there is a difference between  
14 the saline conditioned animal and the high naloxone.  
15 significant  
16 I don't believe there is a/difference here but there  
17 is certainly a difference between the low and the  
18 high naloxone treated animal. That is clear. There  
19 is also a difference between the low naloxone and  
20 the saline treated. That is perfectly clear. I  
21 do not know if there is a difference between the  
22 saline and the high naloxone. That is the only point  
23 I am raising.

24 THE COMMISSIONER: Well Mr. Brown,  
25 correct me if I am wrong, what you are implying is  
in this document is if you treat a digoxin intoxicated  
animal with a low dose of naloxone it will help him





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2 to the extent that it will delay the onset of the  
3 toxicity symptoms. But if you treat him with a  
4 lot of naloxone it will bring it on faster. Is that  
5 what you are implying?

6 MR. BROWN: That was my understanding.

7 THE COMMISSIONER: Do you agree  
8 with that?

9 THE WITNESS: I think that is a  
10 reasonable conclusion from these data in this  
11 experimental situation. One point I would mention  
12 to you, the heart rate again, since it did come up  
13 earlier in the other proposal, if you look at Table 1,  
14 take a look at the basal heart rates here under signal  
15 shock on the left, you see basal, and then you have  
16 NaCl and low naloxone and high naloxone, you will  
17 notice as you go from a controlled situation, the  
18 high naloxone tended to reduce the heart rate.  
19 Essentially as you enhance the digitalis toxicity  
20 you tend to reduce the heart rate. This is apropos  
21 of your previous discussion.

22 Q. Then I take it on the basis  
23 of the temporal relationships observed by the authors  
24 of this paper and on the basis of the heart rates  
25 observed by the doctors in this paper, you would  
not change your opinion as to the possibility of





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2 involvement of digoxin in the death of a child who  
3 is subsequently administered naloxone.

4 A. I do not think I made my  
5 point very clear to you. I am going to go again on  
6 this. I think that the similarity of symptomatology  
7 in no way should be used to infer a similarity in  
8 etiology, period.

9 Q. What I am suggesting to you,  
10 Doctor, is that --

11 THE COMMISSIONER: I did not under-  
12 stand that sentence. You used too big words for  
13 me.

14 THE WITNESS: The similarity in  
15 symptomatology that we see here, the decrease in  
16 heart rate we see here and which we see in digitalis  
17 intoxication does not mean that the events that  
18 occurred in the patient under question were due to  
19 the same causative factors. That is the part I am  
20 not going to be willing to conclude. I hope you  
21 understand that.

22 Q. I am not asking you to do  
23 that. I think what I am ---

24 THE COMMISSIONER: Hold on for a  
25 minute. It is the converse that worries me. If there  
is a dis-similarity it may help. The similarity is





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very common. Digoxin toxicity manifests much the same symptoms as many other diseases but where there is no similarity, that is, where there is something, and this is what I asked yesterday and which you said you did not want to answer and did not feel --

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THE WITNESS: Qualified, I used the term.

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THE COMMISSIONER: I was not going to say that.

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THE WITNESS: I hesitated to say it myself.

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THE COMMISSIONER: That is perfectly reasonable. I am not qualified either. All I can do is get what assistance I can. The other way though may be of some assistance. If the symptoms are not the same as digoxin poisoning it does help us to eliminate those babies from any kinds of suspicious deaths.

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THE WITNESS: I think Mr. Brown has really brought a very interesting avenue of examination of this point. I have said that these findings are very similar to what occurs in digitalis intoxication, but I don't feel that I am able to infer that from the similarity of these events that that is what occurred in this particular patient.





1  
2 Q. Can I put one final set of  
3 suggestions to you. Is it your opinion that death  
4 caused by ideosyncratic reaction of naloxone is rare?

5 A. Correct.

6 Q. On the basis of these two  
7 papers which show to a greater or lesser extent and  
8 with the qualifications you have suggested, a temporary  
9 relationship between the administration of naloxone  
10 to digitalized animals and death, given those papers  
11 and given the rareness of the ideosyncratic reaction  
12 to naloxone, can one say that the observed death  
13 shortly after the administration of naloxone more  
14 likely would have been caused in the presence of  
15 digoxin or would more possibly have been caused in  
16 the presence of digoxin?

17 A. I don't want to appear too  
18 stubborn or immovable on this issue because I think  
19 it is more the intellectual dialogue that intrigues  
20 me. I think that one might come down to that question  
21 with a large number of caveats and restrictions  
22 qualifying it which almost makes a 'yes' meaningless.

23 The concern here that I must raise  
24 is the very scanty nature of the information that  
25 I have on this, but let us accept these two papers





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2 and say that they are valid. A critical issue here  
3 is the concentration of naloxone that was given to  
4 this patient, does it in any way resemble this  
5 stoichiometric relationship achieved here. By  
6 stoichiometric I mean the concentration of naloxone  
7 to digitalis-like drugs that occurred in the  
8 experimental animals, was that achieved in this  
9 patient, assuming that digoxin was indeed present  
10 in this patient. That is part of our scenario.

11 A. One must postulate that  
12 the amount of naloxone given to this patient was  
13 in the range of the high concentration because,  
14 to follow your argument to its inexorable conclusion,  
15 if the amount that we gave to this patient of  
16 naloxone was of the low concentration we would  
17 have protected this patient; so be careful. I do  
18 not think I am able to really give you a "yes" to  
19 your answer for those reasons. I hope you understand  
20 that.

21 Q. Thank you. The second  
22 area I would like to examine you on is another  
23 baby, Janice Estrella. I don't have your chart.  
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This, for simplicity's sake, a child in whom a post mortem reading of about 72 was found and the sample was taken from the pelvic gutter.

At the time you initially conducted the review, Doctor, I believe you were aware of the post mortem reading of 72, it appears at page 26 of your bound report.

A. Yes.

Q. And am I correct in saying that at that time and in view of the magnitude of that sample a judgment was reached that this child's death may have been caused by digitalis intoxication?

A. That is correct.

Q. At the time you conducted the review, did you know the source of that sample which gave the 72 reading?

A. I don't think we did, although it may have been noted in the original document, I can look that up right now, the Cimbura document, it may have been noted there. If I did know it, I think I assumed at the time that it was the serum concentration I may have --

Q. I don't think you will find it in the Cimbura document, I believe this sample was





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assayed at the hospital and not at the Center of Forensic Sciences.

A. Let me just say I assume that it was a serum sample, I believe.

Q. At the time you conducted the review were you aware of any concerns about possible contamination of that sample?

A. No, sir.

THE COMMISSIONER: That is the answer to it. I am just wondering though about -- there is some suggestion that the samples were contaminated in the post mortem. We have always had this trouble because the post mortems are never dated and we don't know when they were given, but in both the -- I take it that that post mortem was long after the event, was it, that autopsy report?

MR. LAMEK: I believe so, Mr. Commissioner, but it was in the chart that was supplied to Dr. Mirkin, page 12.

THE COMMISSIONER: It was in the chart, have you got the chart there?

THE WITNESS: Oh, the baby's chart?

MR. LAMEK: The baby's chart.

THE WITNESS: Yes, I have it here.

MR. LAMEK: Page 12.





1  
2 THE COMMISSIONER: Well, they don't  
3 say where it was taken from, they say the samples  
4 were contaminated slightly by edema fluid and  
5 ascetic fluid. It was afterwards that Dr. Taylor  
6 told us about the bowel having been cut with the  
7 result in the post mortem, with the result there  
8 may have been considerably more contamination.

9 A. Yes, Mr. Lamek discussed  
10 that with me the other day.

11 THE COMMISSIONER: Yes. At any rate,  
12 the answer was you took the 72 as an honest reading.

13 THE WITNESS: Correct.

14 THE COMMISSIONER: And it was not  
15 contaminated?

16 THE WITNESS: Yes, we interpreted  
17 that as a serum sample.

18 Q. And I believe you testified  
19 yesterday that you have heard that the Estrella  
20 data base is now open to some question and that  
21 reduced your confidence in the significance one  
22 could attach to that sample, is that correct?

23 A. To that particular sample.

24 Q. Yes, to that particular sample.

25 THE COMMISSIONER: Yes, to that  
particular sample.





1  
2 Q. Precisely what did you hear  
3 about the data base that reduced your confidence  
4 in the sample?

5 A. I think essentially what the  
6 Commissioner has mentioned, that there was a pos-  
7 sibility of not so much contamination of the sample  
8 perhaps, well, contamination I guess is not a bad  
9 word, but that the drug may have been leached out  
10 of the intestinal canal and into the area from  
11 which this particular sample was obtained, I think  
12 that was the gist of it. When I say contamination,  
13 not that anyone had added anything to the sample  
14 but that this might have been misleadingly elevated.

15 Q. Were you aware that the  
16 sample was taken under the following conditions:  
17 that the autopsy had been performed, the child  
18 stitched up, taken to the morgue; the pathologist then  
19 went down to the morgue, reopened the child and took  
20 the sample at that time, were you aware of that  
21 sequence of events?

22 A. No, sir.

23 Q. I put it to you that that  
24 is what happened. About half an hour, approximately,  
25 after the termination of the autopsy the pathologist  
went down to the morgue, reopened the child and





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2

extracted the sample from the fluid in the pelvic  
or gutter area of the child. Were you aware --

3

4

A. Can I interrupt you for a  
minute?

5

6

Q. Yes, certainly.

7

A. How many hours after the  
death would you say this was?

8

9

Q. The autopsy I think, and I  
will be corrected, it might have been about 11 hours  
after death.

10

11

MR. LAMEK: 11 and a half.

12

Q. 11 and a half hours after  
death.

13

14

THE COMMISSIONER: Three hours  
after that, wasn't it, when --

15

16

Q. Yes, I recall the autopsy I  
think took three to four hours, the late afternoon,  
and about half an hour after the termination of the  
autopsy which had taken about three hours or so the  
pathologist then went down to the morgue, reopened  
the child and drew the sample.

20

21

A. We are talking about a sample  
taken 14 hours, or 11 hours after death?

22

23

Q. 14 to 15 hours after the  
death.

24

25





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2

A. Oh.

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Q. Were you also made aware of a study conducted by the Hospital for Sick Children and the Center of Forensic Sciences in which an effort was made to replicate the conditions under which the sample from this child were taken?

A. Yes, it was brought to my attention, you could perhaps repeat the data.

THE COMMISSIONER: It was one that was wildly out of line, out of about ten, what is the number?

MR. LAMEK: 14.

Q. Perhaps I could ask the Registrar to show you Exhibit 238. The exhibit consists of a covering letter from Mr. Cimbura to Dr. Phillips at the Hospital, and the second page contains the result of what we know as the gutter blood study. Have you seen the results of the study in that form before?

A. No, sir.

Q. The effort made by the hospital and the Center of Forensic Sciences to replicate the conditions under which the Estrella samples were taken involved the development of an autopsy protocol. We have heard that although the protocol does not





1  
2 duplicate in complete identity the circumstances  
3 under which the sample was taken, it is very similar.

4 The autopsies performed on the 14  
5 children you see listed here involved the taking of  
6 a blood sample at the beginning of the autopsy, from  
7 the heart, and from the sagital sinus. These samples  
8 were subsequently subjected to testing by RIA and  
9 you see the results right there.

10 There are then two other columns,  
11 the first column is entitled: "Gutter No. 1,"  
12 and that indicates a sample taken from the child  
13 from the pelvic cavity, during the course of the  
14 autopsy. The samples were similarly assayed by  
15 I believe RIA only and you have the results there.  
16 The readings found in the column headed: "Gutter  
17 No. 2" were taken from -- the samples were taken  
18 three hours after the end of the autopsy, and again the  
19 samples were taken from the pelvic cavity area, from  
20 the same area in which the samples shown in "Gutter  
21 No. 1" column were taken. That generally was the  
22 protocol of the experiment.

23 You can then see the results under  
24 "Gutter No. 1 and Gutter No. 2", a total of 25  
25 assays were run of the samples taken from these  
14 children. As you can see from the samples under





1  
2 "Gutter No. 1" there is one, case No. 5, which  
3 sticks out significantly and in that case the ratio  
4 between the reading in the gutter blood and the reading  
5 in the heart is about 17 to 1.

6 Now, am I correct in saying that it  
7 was probably that reading which called into question  
8 in your mind the significance and the validity of  
9 the Estrella sample?

10 A. No, this is the first time  
11 I have seen this, so it didn't --

12 Q. Perhaps I can go one step  
13 further.

14 A. I am not sure what you mean  
15 by that question. Are you referring, have I had a  
16 chance to review this?

17 Q. You said at the beginning you  
18 had not seen this table before.

19 A. No, I have not, correct.

20 Q. If you look at "Gutter No.  
21 1."

22 A. Yes.

23 Q. And the results there.

24 A. Yes.

25 Q. Those are samples taken from  
the pelvic cavity during the autopsy; and we have the





1  
2 results from 14 children. These calculations have  
3 not been put into evidence before, and I am sure they  
4 will be subject to scrutiny by others. With the  
5 exception of case No. 5 where we see that very high  
6 reading, the ratio of the concentration of digoxin  
7 found in the pelvic cavity to the concentration of  
8 digoxin found in the sample of blood taken from the  
9 heart ranged from a ratio of a low of 0.6 to a  
10 high of 2.6. So there was a variation from slightly  
11 under 1 to about 2-1/2 times what was found in the  
12 heart, the average was about 1.3. There was one  
13 case, and that was case No. 5, where that same  
14 ratio was 17.1.

15 A. Okay.

16 Q. Okay. So that was the  
17 result on the samples taken during autopsy from the  
18 pelvic cavity.

19 You have column No. 2, gutter No.  
20 2, these were the samples taken three hours after the  
21 end of the autopsy. Now, the ratios between the  
22 concentration of digoxin in the pelvic cavity to the  
23 concentration of digoxin found in the heart sample  
24 in the samples taken three hours after the end of the  
25 autopsy range from a low of about 0.5 to a high of  
about 2.05, with an average of about 1.3.





10  
1 So of the 25 samples that were  
2 taken and form the basis of what we know as the  
3 gutter blood study, for 24 of the samples the range  
4 of ratio between pelvic cavity blood and heart blood  
5 range from about 0.5 to 2.6, because that was really  
6 one of the findings of the study.

7 There was one case, one out of the  
8 25 in which the ratio was 17.1. If I can draw your  
9 attention to that case, case No. 5 on the chart,  
10 the sample which was taken, the first sample taken  
11 from the pelvic cavity, the ratio was 17 to 1,  
12 three hours later they took another sample here,  
13 same area, same child, and the ratio was 1.8.  
14 Now, were you aware that there had been 25 different  
15 assays done?

16 A. I said no.

17 THE COMMISSIONER: I think it is 26.  
18 I hate to interrupt this long question of yours, but  
19 it is 26, is it, and not 25? It doesn't matter  
20 anyway. He wasn't aware of this experiment at all.  
21 Your question surely is just this change --

22 MR. BROWN: Yes, if I can just  
23 continue.

24 Q. I put it to you that of the  
25 25 or 26 all but one demonstrated a ratio in the range





1

2

of 0.5 to 2.6. I have indicated to you that in one  
case the initial sample demonstrated a range of  
17 to 1, when another sample taken three hours  
from the same baby was assayed and the ratio  
demonstrated was 1.8.

6

7

Now, on the basis of that information,  
does that in any way change the confidence that you have  
in the sample taken from Janice Estrella?

9

A. I think --

10

11

THE COMMISSIONER: Surely you mean  
the lack of confidence, don't you, not the confidence,  
he has indicated --

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G-1  
M/PS

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MR. BROWN: He has little confidence

3

in it.

4

THE COMMISSIONER: Yes. Well, now,

5

does it change your view, and I think your view was

6

the lack of confidence.

7

THE WITNESS: Yes, based on the

8

information I had received that there were questions

9

about the validity of that particular point. I think

10

what you should be aware of though is that when we  
reviewed this -- well, let me say this much. Reading

11

these data certainly make me question whether the

12

lack of confidence in those data in the 72 value is

13

warranted. I think that indeed may be an accurate

14

reflection of what was there; let's make that a

15

point. Because now one would have to reconsider why

16

one would call that particular value unreliable in

17

the face of the study you have just presented which

18

suggests that the gutter levels, whether taken at

19

the post or three hours thereafter are really a

20

very accurate reflection of what is in the heart

21

blood or the sagittal sinus-- well, or the heart blood,  
let us say.

22

Q. In the face of the results of

23

that study ---

24

MR. LAMEK: Let him finish the answer.

25





1  
2 THE WITNESS: Well, no, let me  
3 finish now.

4 MR. BROWN: Q. Oh, I'm sorry, if  
5 you haven't finished, please do so.

6 A. The point I am making is that  
7 these data suggest that the gutter blood may  
8 actually be an accurate reflection of what was in  
9 the systemic blood of this patient. Okay, is that  
clear?

10 Q. Yes.

11 A. I think it is important though  
12 for you to understand that our evaluation at the  
13 time I made it, also made that presumption that the  
14 72 was a valid number.

15 Q. Yes.

16 A. Okay. So, now one can go  
17 back to accepting those data with more confidence as  
a consequence of these data.

18 Q. Am I correct then in saying  
19 that your present opinion is that you would have  
20 confidence in the reading obtained from the Estrella  
21 sample?

22 A. More confidence, certainly,  
23 than I have been led to believe was warranted since  
24 my arrival here. Unless the Estrella sample turns  
25





1  
2 out to be one in the 25.

3 Q. Well, on the basis of your  
4 present understanding then of the gutter blood  
5 study and on the basis of your present confidence  
6 in the Estrella sample, what is your opinion as to  
7 the possible involvement of digoxin in the death  
8 of Janice Estrella?

9 A. I think it leads us to a  
10 higher likelihood that her death was associated  
11 with that high blood level.

12 Q. Is that degree of likelihood  
13 in your opinion of a similar magnitude as the degree  
14 you showed in the case of Cook, Miller and Pacsai?

15 A. I think so.

16 Q. Okay. I have no further  
17 questions, Doctor. Thank you.

18 THE COMMISSIONER: Ms. Forster,  
19 do you want to go now or do you want to wait until  
20 after the break?

21 MS. FORSTER: I think I would prefer  
22 to wait until after the break.

23 THE COMMISSIONER: Yes, all right.  
24 Well, then, we will take 20 minutes now then but that  
25 means that we will be back at a quarter to 12.

---Short recess.





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---Upon resuming.

3

THE COMMISSIONER: Yes, Ms. Forster.

4

MS. FORSTER: Thank you.

5

CROSS-EXAMINATION BY MS. FORSTER:

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Q. Dr. Mirkin, my name is

Elizabeth Forster and I act on behalf of Nurse

Phyllis Trayner. You indicated yesterday, Doctor,

that all of the members of your team except for Dr.

Moller were clinical pharmacologists, is that correct?

A. That is correct. They are all

pediatricians who are practicing physicians who

work with intensively or acutely ill children.

Q. That was my next question.

Do you and your associates, leaving aside Dr.

Moller for a second, do you carry a full patient

load or do you act as consultants to other doctors?

A. I am in charge of a ward at

the University Hospital. My other colleagues also

serve as attending physicians on their own respective

wards. We occasionally bring in private patients but

as clinical pharmacologists in that capacity we act

as consultants, at other times we act as participat-

ing members of the Department of Pediatrics and

fulfill regular patient care responsibilities.

Q. All right. Dealing first with





1

2

your ward responsibilities. Are you in charge of the  
cardiology ward?

3

4

A. No.

5

Q. Are any of your associates?

6

A. Dr. Green has many cardiac  
patients on the juvenile or intensive care unit.

7

In embellishing that a bit I have patients with

8

cardiac problems on my ward, but I am not the

9

referring physician or the primary physician for

10

most of these patients.

11

Q. All right. Dealing with your  
functions as a clinical pharmacologist in which you  
consult for other doctors, do you consult with  
respect to pediatric cardiology patients?

12

13

14

A. That is correct.

15

16

Q. And what percentage of your  
time would be taken up in consulting with that type  
of patient, the pediatric cardiology patient?

17

18

A. That is very difficult to say;  
10% perhaps.

19

20

Q. All right. Now, dealing with  
your report, Doctor. I take it that one of the  
things that you were asked by this Commission to do  
was to determine whether there was any evidence of  
digoxin intoxication present during the childrens'

21

22

23

24

25





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2

hospitalization at the Hospital for Sick Children,  
is that correct?

3

4

A. That is correct.

5

6

Q. And in fact the scoring that  
we see on pages 3 and 4 of your report relate to this  
particular task.

7

8

A. That is correct.

9

10

11

Q. And I take it from evidence we  
have heard in these proceedings that digoxin intoxica-  
tion is not that uncommon among patients who are  
on digoxin therapy, is that correct?

12

13

A. Well, I am not sure what you  
mean by that, uncommon.

14

15

16

Q. Well, it was my understanding  
that if a patient is on normal digoxin therapy it  
is not a rare occurrence to find that they show  
some signs of intoxication from time to time.

17

A. I guess that is acceptable.

18

19

20

21

Q. And did it come as any surprise  
to you to find that in this population of some 36  
pediatric cardiology patients some of them did in  
fact show signs of digoxin intoxication at their  
stay at the hospital?

22

A. No.

23

24

25

Q. Okay. Now, in reviewing the





1  
2 babies' charts and the zebra packs to find evidence  
3 of digoxin intoxication during the period of  
4 hospitalization, did you look at all of the symptoms  
5 shown by the babies right up until the time they  
6 were declared dead?

7 A. We attempted to.

8 Q. And would that include the  
9 terminal events exhibited by the children?

10 A. In attempting to develop  
11 this score?

12 Q. Yes.

13 A. Yes.

14 Q. In cases where there was no  
15 ante mortem digoxin levels you were dealing simply  
16 with the clinical symptoms, how in your scoring did  
17 you treat terminal events that were consistent both  
18 with the child's clinical condition and digoxin  
19 intoxication?

20 A. It was a very difficult  
21 discriminatory process. I think when you talk about  
22 terminal events I think that one has to distinguish  
23 between events that occur at the time resuscitation  
24 is initiated, which is maybe when cessation of the  
25 heart occurs or breathing, but what we attempted  
to do was to analyze the course of events during that





1  
2 last week, as you saw from our review data sheets,  
3 and to identify specific problems that the patient  
4 presented that could or could not have been associated  
5 with the diagnosis of digitalis intoxication.

6 We attempted wherever possible to  
7 employ the criteria described earlier in testimony  
8 which I think are rather standard criteria for  
9 making this diagnosis. But to say that it was  
10 absolutely possible to isolate problems attributable  
11 to the basic disease of the patient from those that  
12 were attributable to digoxin, where those were very  
13 similar was, of course, it is an impossible  
14 statement to comment on. We obviously were not  
15 able to separate those out 100%.

16 Q. I wonder if we could deal  
17 with a couple of specific children in this regard.  
18 First of all, Justin Cook. You had initially rated  
19 Justin Cook as a zero based on your understanding  
20 that the level of 72 was a post mortem level, as  
21 I understood your evidence yesterday.

22 A. That is correct.

23 Q. And then when you found out  
24 that the level of 72 was in fact taken, the sample  
25 was drawn during resuscitation efforts, you re-rated  
the child to a 9. I take it obviously that the only





1  
2 factor that affected your change there was the  
3 knowledge that that level of 72 was in fact an  
4 ante mortem level.

5 A. I think that's correct.

6 Q. And the symptoms or the terminal  
7 events displayed by this child were consistent, as  
8 I understand it, both with this clinical condition  
and with digoxin intoxication.

9 A. I think that is reasonable.

10 Q. And in the absence then of  
11 the ante mortem level, having regard to those  
12 symptoms, you still rated the child as a zero in the  
13 absence of the level of 72.

14 A. Yes, because we felt that the  
15 evidence, that the cause of these symptoms was more  
16 likely due to the basic disease of the patient rather  
17 than the drug since there was no evidence of the drug  
being present in excessive amounts.

18 Q. Okay. Dealing then with Baby  
19 David Taylor, which was your code number 1, and is  
20 found at page 121 of your report. Again, with this  
21 child we have no ante mortem digoxin levels  
22 and you list at page 123 of your report those factors  
23 which you found to be evidence of digitalis intoxica-  
24 tion.  
25





1

2

A. I don't have that document.

3

123 is the last page?

4

Q. Yes.

5

A. Is this what you are referring

to?

6

Q. It is paragraph 5 in David

7

Taylor and you have coded David Taylor as patient

8

number 1.

9

A. That is correct.

10

Q. Okay.

11

A. Yes, okay.

12

Q. Paragraph 5 where you list

13

evidence of digitalis intoxication.

14

A. Yes.

15

Q. All right. What is listed

there is variable of 2 to 1 AV block.

16

A. Okay.

17

Q. You've got me?

18

A. Yes.

19

Q. Okay. Now, as I see it the

20

factors that you say are evidence of digitalis

21

intoxication are the same as the terminal events

22

which you list on the first page of the David Taylor

23

report under paragraph 3-B.

24

A. Yes.

25





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4

Q. So, basically then the terminal events shown by this child, that led your group to categorize this child as a 9?

5

6

A. I think that is reasonable to conclude, yes.

7

8

9

10

11

Q. And we have heard evidence from both Dr. Rowe and Dr. Izukawa from the Hospital for Sick Children that the terminal events displayed by this child were consistent not only with digoxin intoxication but with his clinical condition. Is that something with which you would agree, Doctor?

12

13

14

A. Well, I don't know whether one would conclude that this is characteristic of patients who have aortic stenosis, I am not sure that this is correct.

15

16

17

18

Q. All right. Can you tell me then what symptoms he displayed which you say are inconsistent with the condition of the aortic stenosis?

19

20

21

22

23

24

25

A. Well, I'm not sure that one would be expected to find an atrial ventricular block with this Wenckebach phenomena I discussed.





H  
DP/PS

1  
2 I think what you see here is a patient  
3 who is showing some degree of blockage and it is  
4 a question of whether or not this patient's  
5 basic disease, which included not only aorta  
6 stenosis but endocardial fibroelastosis, whether  
7 or not that latter component of this symptom complex  
8 was affecting the conduction pathway in this patient.  
9 If one makes the presumption, as the other two  
10 consultants obviously did, that the conducting  
11 pathway is affected by the disease, then one could  
12 postulate I suppose that this arrhythmia might be  
observed in that situation.

13 I think, though, that the kind of  
14 judgment that is made here perhaps depends on  
15 what kind of emphasis you want to present on the  
16 etiology of the symptoms, I suppose. If one takes  
17 the view that this more likely reflects digitalis  
18 intoxication rather than intrinsic disease, you come  
19 out with the conclusion we did. If you take the  
20 other position then you can come out with the other  
21 conclusion. The balance here is whether or not this  
22 is more typical, in my mind, of digitalis intoxica-  
23 tion than of phenomena associated with the intrinsic  
24 disease the patient had. I think we collectively  
25 opted for the latter.





1  
2 Q. Just so I am clear, Doctor,  
3 when you say you are looking at whether or not  
4 it is more typical of digoxin than the inherent  
5 disease, are you talking again about the AV block  
6 and the Wenckebach block?

7 A. I think we are talking about  
8 the rhythm changes primarily. You know, there are  
9 some early signs here. This patient was vomiting,  
10 showed emesis, which could be used as a softer sign  
11 of digitalis intoxication that one would not, at  
12 least in my opinion, have anticipated that this  
was due to the basic disease alone.

13 Q. Is there anything else in  
14 this child's condition that you can point to that  
15 you say is inconsistent with his clinical condition?

16 A. I don't think anything of  
17 major significance.

18 THE COMMISSIONER: I guess you have  
19 given us this, Doctor, but when a score is 9 I  
20 had understood that that was only the sort of  
21 symptoms up to but not including the terminal  
22 symptoms. Now you are saying it is the terminal  
23 symptoms as well. But if you include the terminal  
24 symptoms -- I take it the only reason this is an  
25 unexpected death is because the baby was, in your





1  
2 collective opinion, suffering from digoxin intoxica-  
3 tion at the time of death. But he was not included  
4 in the summary that you gave Mr. Lamek as one that  
5 died from digoxin toxicity. Is that only because  
6 you do not have any toxicology?

7 THE WITNESS: I think this is  
8 primarily the issue here.

9 THE COMMISSIONER: But if you had  
10 to choose, if you had no pathology given to you at  
11 all and you had to choose between death from natural  
12 causes and death from digoxin toxicity for this  
13 baby Taylor, you would choose the digoxin, I take  
14 it.

15 THE WITNESS: I think I might.

16 THE COMMISSIONER: I said, "would".  
17 You said, "might". Is there a delicate distinction  
18 there?

19 THE WITNESS: Fragile distinction.

20 THE COMMISSIONER: All right.

21 THE WITNESS: I would say that the  
22 burden of proof would be to prove that the patient  
23 did not die from digoxin. I think there is a greater  
24 likelihood here of that being involved in the final  
25 events than not.

THE COMMISSIONER: You see, the problem





1  
2 we are faced with is that that is fine for Taylor  
3 and that perhaps helps us, because that is your  
4 opinion, but all the other high readings, Gage,  
5 McKeil, and we have Estrella already, but Gage,  
6 McKeil and perhaps we have had Gosselin already,  
7 I don't know whether those high readings are based  
8 upon events that may have taken place any time in the  
9 last seven days before death or the terminal events.  
10 The terminal events mean a lot more to me than the  
11 earlier events. Can you tell us, with respect to  
12 Gage and McKeil.

12 THE WITNESS: I really will have to  
13 review each of the charts and perhaps I could do that,  
14 if you would like. I certainly will try.  
15 Off hand, I cannot. I just want to look through the  
16 charts, my records, and see what events were present  
17 and the time at which they were present. We felt  
18 that all of the events in the last seven days of  
19 life would be of importance.

19 THE COMMISSIONER: They would be of  
20 importance, but you see the suspicion here is of  
21 a massive overdose given shortly before death and  
22 the result of that massive overdose being death of  
23 the child. So what might have happened four or five  
24 days before, and the child recovered from it, is  
25





1  
2 unlikely to have affected -- perhaps I am wrong but  
3 I would have thought would have not affected the  
4 death.

5 THE WITNESS: Yes and no. I would  
6 agree with you that the events in the last day or the  
7 last few hours are really very crucial here, certainly.  
8 One could easily postulate, and I think this is  
9 probably not out of keeping with reality, that  
10 a patient who became intoxicated early in the course  
11 might on a subsequent re-exposure, re-challenge  
12 to the drug, have a tendency to become more readily  
13 intoxicated later on. So we felt that that informa-  
14 tion was useful.

15 I imagine if one were to go back and  
16 rework all of the data it would be impossible to  
17 identify those cases in which the score was  
18 predicated on very, very late events and those  
19 in which we saw intoxication earlier on, in the  
20 last week of life, let us say.

21 THE COMMISSIONER: Have you any doubt  
22 with respect to Taylor? Ms. Forster is putting to  
23 you that the Taylor rating is based on the terminal  
24 events. Is there any doubt in your mind it might  
25 have been based on something else?

THE WITNESS: No, I think that most of





1  
2 the information we have here occurred in the last  
3 two days of life. On 7-27, just looking now at our  
4 information.

5 THE COMMISSIONER: 7-27, what is that?

6 THE WITNESS: That is actually the  
7 day of death.

8 THE COMMISSIONER: I see. That is  
9 the 27th of July.

10 THE WITNESS: Yes, July 27th.

11 We have here that the patient vomited and shortly  
12 thereafter demonstrated a very rapid heart rate with  
13 varying degrees of atrial ventricular block and went  
14 into ventricular fibrillation.

15 The patient -- Dr. Freedom, who  
16 is he?

17 MS. FORSTER: Dr. Izukawa  
18 attended. Dr. Freedom is also at the hospital, yes.

19 THE WITNESS: Okay, good. We have  
20 his comments here that the patient was moderately ill,  
21 had severe aortic stenosis but reasonably functioning  
22 left ventricular. This is Taylor I am talking about.  
23 You have a patient here who is described by someone  
24 who is immediately on site as being moderately ill  
25 and had some difficulty in breathing. We have what  
I would describe as very, very strong evidence in the





1  
2 electrocardiogram for digitalis effect and block  
3 and toxicity and I don't know what else to say.  
4 If one argues that arrhythmia could also be found  
5 with the endocardial fibroelastosis and one might  
6 argue that, then it is going to be a judgment call  
7 but I think our judgment is better than others.

8 Q. Did I understand, Doctor, from  
9 what you said to the Commissioner a few minutes ago  
10 that in your opinion there is a greater likelihood  
11 that this child died from an overdose of digoxin  
12 than died of his clinical condition?

13 A. Well, I was inferring that  
14 if indeed this is digoxin intoxication at the terminal  
15 event, then I would conclude it was contributory to  
16 the patient's demise to a large degree. This does not  
17 preclude what role the basic disease played in this.  
18 I think it is difficult to isolate them. If you  
19 asked me, would the patient have died from the disease  
20 alone without the drug at that time, I would have to  
21 say no, but that again is an imprecise answer.

22 Q. When we are talking about  
23 the digoxin being contributory to death, are you able  
24 to tell us whether you are talking here about intoxica-  
25 tion as a result of this digoxin therapy or whether  
we would have to be talking about an overdose of digoxin?





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A. Well, regardless of how the drug or the amount that was given, there appear to be circumstances in this patient in which an excessive amount of digoxin has either accumulated or this particular patient appears to be unusually sensitive to what might be normal levels of digoxin. I have no way of knowing, but my recollection is in this patient we had no measurement, is that correct?

Q. Yes.

A. To answer your question as briefly as I can, it is conceivable that digitalis intoxication incurs as a consequence, you know, associated with administration of what we will call correct doses of the drug. That could occur. It is equally as possible it could have occurred as a consequence of an overdose.

Q. It could be either?

A. I think so.

Q. Finally, yesterday when you were discussing the involvement of digoxin deaths of various children you had three categories, and the first category was one where you thought it probable that digoxin caused death in the Miller, the Cook and the Pacsai babies. You had another category involving Kristin Inwood where you said it was conceivable it





1  
2 was digoxin but also conceivable the child died of  
3 potassium, and another category where you said  
4 digoxin could have contributed to death and the babies  
5 you placed in that category were the ones where  
6 digoxin was found in post mortem tissue and the child  
7 had not been prescribed digoxin. In which category  
8 would you place Baby Taylor or would you place him  
9 in any of these categories?

10 A. If we must label him, I guess  
11 I would put him in the conceivable group. Is there  
12 a conceivable group?

13 Q. The baby that you have in the  
14 conceivable group was one where you said it is con-  
15 ceivable that the child died of potassium and it is  
16 also conceivable that the child died of digoxin.

17 A. Well, we had better not be  
18 so ambiguous. I think I am going to make a possible.  
19 Is there a difference between a probable and a  
20 possible?  
21  
22  
23  
24  
25





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I: 2  
DM: 3  
yk 4

Q. Is there in your mind -  
what is in your mind important, how would you classify  
this child?

4

5

A. I would say that it is very  
possible that digitalis was involved in the death of  
this child.

6

7

THE COMMISSIONER: Can we put very  
possible, fairly probable do you think? We have  
tried it out on the scale of 1 to 10 before, does  
that help you at all, or would you rather not answer  
that.

11

12

THE WITNESS: I really would rather  
not if you don't mind.

13

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Q. Next dealing with baby  
Woodcock; baby Woodcock was given a score of zero  
by your team, and again in finding on that score  
you considered the terminal events displayed by this  
child?

18

19

A. If you don't mind I will have  
to get my notes on that.

20

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Q. She is your Code No.25.

A. Yes, I know. I am going to  
take a moment to see if I can find this patient's  
EKG data if you don't mind. Do you know if there  
was a zebra chart on this patient?





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2

MR. LAMEK: Woodcock?

3

THE WITNESS: Woodcock.

4

MR. LAMEK: I think so.

5

Q. She doesn't appear to be  
included in the summaries of Dr. Moller.

6

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A. No, I know it is not there  
but I have my own notes on the electrocardiographic  
information. This particular patient as you know  
had a primary diagnosis, pre mortem diagnosis of  
cholestasis, that is the patient had jaundice, and  
the post mortem diagnosis showed pneumonia  
bilaterally, and those were the major findings.

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The primary events that occurred  
in this particular patient were really related to  
this child's feeding difficulties and enlarged  
liver, which were noted on June the 26th of 1980.  
On June 30th, which was really the first signs of  
the symptoms compatible with dig. intoxication,  
the child had emesis at 3 o'clock in the morning  
and an irregular heart rate. At 6 o'clock that  
morning the child had complete heart block with  
AV disassociation, which was compatible in our  
mind with the diagnosis of digitalis intoxication.  
At 9:30 the patient arrested.

Now in this particular circumstance





1  
2 it is clear that this patient did not - the diagnosis  
3 would not have been made -- This is interesting,  
4 I see complete heart block here and I would have  
5 concluded that this patient - one might have thought  
6 this patient had some digitalis, this is interesting.  
7 The patient, you see we concluded a zero on this,  
8 okay, now I think it is important because there was  
9 no digitalis on record, okay, none in this particular  
patient, correct?

10 Q. Yes.

11 A. So that was another factor  
12 as you read my introductory comments on the  
13 preparation of this score, that we based this on  
14 clinical data in the chart. Based on that information,  
15 since the patient had received no digitalis officially  
16 I think we concluded that this patient was not  
17 digitalis intoxicated. Also June 28th, okay, June  
18 28th, this is two days prior to death, the patient  
19 had - the EKG was read as a normal sign as written,  
20 normal rate and we could not see any digitalis  
21 effect, it is important. Now I don't have Dr. Moller's  
22 official reading of that electrocardiogram and I  
23 would like to request that if I may to look at it  
24 myself, or perhaps call Moller and see if he did  
25 review that and didn't append it. But my notes, this





comment about June 28th when the electrocardiogram was normal is based on notes taken from our very intensive review of the case during our team meeting, okay?

Q. Yes.

A. And two days after this electrocardiogram the patient died. Now, I don't know if we have any other electrocardiographic tracings on this patient. They must have, because in our notes and in the chart there is a comment, there must be EKG's on this patient, because we have the comment here:

"Patient had complete heart block and AV disassociation."

And that would have been made with electrocardiographic tracing, now this is three hours before death.

Now I think that with the appearance of these symptoms at 3 a.m. on the morning of June 30th, one would be tempted to conclude very strongly that this reflects the digitalis effect in this patient, and our zero score, as I look at it now, was predicated on the premise this patient never received digoxin, is that clear?

Q. Yes.

A. Good.





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Q. And I take it then the difference between a baby like Woodcock and a baby like Taylor is the fact that Taylor was in fact prescribed digoxin, there is a record of digoxin administration on the chart?

A. The difference in what context?

Q. In the fact that Taylor you gave 9 to and Woodcock was a zero, even though both of them show the terminal events, are quite consistent with the administration of digoxin, the significant factor in giving one a 9 while the other got a zero if that one was on digoxin therapy and the other one does not appear to have been prescribed digoxon.

A. Also that is one factor, but also what must be remembered there is a more significant cardiac lesion in the Taylor child. Now that of course makes for a more complicated interpretation, does it not when you have disease, cardiac disease plus the possibility of digoxin intoxication. In the Taylor child we concluded that the digoxin was more likely - toxicity was more likely to explain these events than the disease.

In this patient the disease really doesn't explain it. Patients with jaundice and even





1  
2 severe liver disease do not have their heart suddenly  
3 stop as a rule unless there is something in that  
4 chart that I am unaware of and that our team missed.

5 Q. Then I am afraid you have  
6 lost me Doctor. I don't understand why one would be  
7 rated a 9 and one would be rated a zero?

8 A. Well -- Well the basis was  
9 the importance placed on the possibility - on the  
10 presumption that this patient did not receive any  
11 drug. Now if the patient is officially noted not  
12 to have received drugs why attribute the symptoms  
13 to that drug unless we are engaging in a pursuit  
14 to say someone gave that drug, and that was not the  
15 intent of this review are you well aware.

16 Q. But then doesn't that mean  
17 that the difference between the way you came about  
18 giving Taylor a 9 and Woodcock a zero is that you  
19 assumed Woodcock wasn't getting digoxin and you  
20 knew Taylor was getting digoxin, it said so in the  
21 chart.

22 A. Hmm.

23 Q. So it enabled you to make  
24 an assumption that digoxin intoxication could be --

25 A. That was one of the factors  
certainly, but don't infer I think that it is the only





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factor, you said only and it is not the only.

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Q. Well in both cases we have terminal events which are consistent with digoxin intoxication?

6

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A. Now you have, six hours before death is not terminal unless you want to define terminal for me, go ahead?

9

10

11

Q. You are the doctor, you define what you mean as terminal.

12

13

A. Well, I think we had better get that clear.

14

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Q. What are you defining as terminal?

19

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A. The events as terminal can be defined as those symptoms occurring at a finite time before cardiac arrest and how far back do we go? Terminal to me means the end. If you say terminal really it is an incorrect use of that term, and doctors always engage in jargon as you know.

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THE COMMISSIONER: No more than lawyers.

THE WITNESS: No more than lawyers. Well I think this is important that we get some precision on it, not to get too polemic on it. How far back do we go? Now, this patient presented at





1  
2 3 a.m. with vomiting and irregular heart rate.

3 If the patient dies six-and-a-half hours later I  
4 would assume that no one in this hospital, or the  
5 doctor in charge did not call the patient, the family,  
6 and say your baby is in a terminal stage of life  
7 merely because that child was vomiting, probably  
8 not.

9 THE COMMISSIONER: Doctor, wouldn't  
10 terminal be anything that led up in a continuing  
11 line to death, that might be five minutes, it might  
12 be five hours, it might five days, or even five  
13 months. When we talk about terminal illness --

14 THE WITNESS: Yes.

15 THE COMMISSIONER: ... one that is  
16 naturally progressive. If there is a recovery from  
17 it then it clearly isn't terminal, even though there  
18 may be another - isn't that, that is what we consider  
19 terminal, do you consider that in the same way?

20 THE WITNESS: I think that is  
21 probably not an unreasonable approach but if terminal  
22 really becomes part of this lengthy continuum,  
23 all of the symptoms then that we find are in the  
24 terminal phase, correct?

25 THE COMMISSIONER: Certainly with  
some of these babies there was a stable condition  
and then there was a sudden deterioration and death.





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Now the terminal events would be from the sudden deterioration, for some of these babies it was a slow decline, obviously some were suffering from a disease but not what I would call terminal. At some point, and it might have been months, or even years before, and I will consider all of those events from the point of the start of the deterioration, and it might even be I suppose at birth but it could be a terminal case from birth that would perhaps not terminate for five years, I don't know, it is something that is inoperable and will eventually inevitably result in death, isn't that terminal?

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THE WITNESS: Well, I guess, you know, the term terminal used in that light applies to everyone in this room. We are all terminal cases from birth on. But I think, yes, I understand that and I don't mean to be facetious or difficult.

THE COMMISSIONER: It is not imminent, at least I hope it isn't and I hope for the sake of all the money we are spending here that in my case it isn't imminent.

THE WITNESS: Well, I certainly hope it's not because we couldn't do this without you, Mr. Commissioner, but I do think that for the purpose of this exercise that what we are interpreting as terminal are probably some of the acute events that occur prior to the demise of the patient. Is that part of your thinking or not? Did you hear what I said?

MS. FORSTER: Q. Yes. When I am talking - let's talk instead of defining it as terminal then. In Woodcock's case, the events from 3 a.m. on.

A. I think that's not unreasonable.

Q. They are consistent with digoxin intoxication?





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A. I think many of them are,

3

yes.

4

Q. And looking at Taylor for a

5

moment, who is at page 121, your Code 1?

6

A. Yes.

7

Q. The events that you have

8

listed on the first page from July 27th starting at

9

ten after midnight with vomiting, those symptoms

10

are all consistent with digoxin intoxication?

11

A. I think they are.

12

Q. Okay. So that the difference

13

between the two then is that one is prescribed

14

digoxin and one isn't?

15

A. I think I would be willing

16

to accept that, I think I have said that earlier.

17

Q. Yes. And in analyzing

18

Woodcock then you went on the assumption that the

19

child didn't receive digoxin because there was no

20

indication of it in the chart?

21

A. That is correct.

22

Q. But in doing the second part

23

of your analysis where you determine the possibility

24

or probability of digoxin causing the death of

25

children, I take it you didn't make any assumption

26

that if digoxin wasn't prescribed it wasn't given?

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A. Yes. If I understand you

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correctly the reason this child was not - well, this

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child was asterisked you know.

5

Q. Yes.

6

A. And we thought that this child

7

had an unexpected death in our minds and we couldn't

8

understand this. Now, if it turns out that we look

9

for cause we raise the question, I think it must be

10

raised, that something caused these changes and

11

the likely culprit in my mind would be digoxin.

12

Q. All right. Now, I want to

13

deal with one general part of your report. If

14

we could turn to, let's say, page 147, at paragraph

15

6 of your report on Woodcock dealing with drug

16

infractions.

17

A. It looks blank.

18

Q. Yes.

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A. Yes.

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Q. You indicated yesterday that

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you broke down the drug interactions between agents

22

influencing digoxin concentration and agents altering

23

sensitivity to digoxin?

24

A. Well, we tried to, yes.

25

Q. Now, dealing first with the

ones that alter sensitivity, and you have listed a





1  
2 few examples, are those ones that make a patient  
3 more sensitive to the effects of digoxin?

4 A. Not necessarily.

5 Q. Okay. What about diuretics,  
6 what effect do they have, do they make one more  
7 sensitive or less sensitive?

8 A. Well, they may if they produce  
9 the proper effect, that is, cause the loss of certain  
10 substances in the body. They may tend to make the  
11 patient more sensitive to the digoxin.

12 Q. Okay. And what about --

13 A. Now, that is contingent.  
14 Not the mere presence of the diuretic in the body  
15 or its administration, that is contingent on the  
16 diuretic causing a decrease in the serum and inter-  
17 cellular level of potassium as you have heard no  
18 doubt.

19 Q. Yes. And adrenergic  
20 agonists?

21 A. Yes. Now, those are things  
22 like adrenelin and other things that were used in the  
23 resuscitation effort occasionally, there are a whole  
24 host of drugs like that. Those drugs generally increase  
25 the sensitivity of the heart to digitalis.

Q. And the adrenergic antagonist





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would decrease the sensitivity?

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A. Decrease it. The best example of that is propranolol that was used in the other patient.

5

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Q. All right. And what about anaesthetics?

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A. There are some anaesthetics.

Now, I don't think they are applicable to any of the patients in this group but these are general anaesthetics. For example, halothane, anyone have an operation? Anyway, those are general gashes anaesthetics which make the heart very sensitive to a variety of different drugs.

14

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Q. Including digoxin?

A. Probably digoxin is one.

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Q. What about the agents that influence digoxin concentration, how do they work?

A. Well, presumably these are drugs that tend to compete with digoxin for the sites at which digoxin bind or where digoxin is stored in the body. If you visualize this being tissue and the digoxin comes and sticks here, if a drug like quinidine is put in, it may come and try to stick to the same spot and displace the digoxin which then circulates and the level goes up





1  
2 for a period of time. Whether that is precisely the  
3 way it works, it may not be certain but I think this  
4 is the general thought on its activity.

5 Q. But it would actually increase  
6 the serum level of digoxin?

7 A. I believe this has been shown  
8 to occur in a sufficient number of cases, to conclude  
9 that it does occur.

10 Q. Is there anything to indicate  
11 by how much it would increase the level?

12 A. It varies on whom you speak  
13 to about this but there have been case reports in  
14 which digitalis intoxication has presumably been induced  
15 by a concurrent administration of quinidine. Then  
16 there is a large school of thought that says this  
17 is one of those, another large school of thought  
18 says this is one of those phenomena that does not  
19 lead to much in the way of clinical consequence.  
20 We can run it either way. But then one has to go  
21 by the data.

22 Q. All right. And did  
23 quinidine, verapamil and antibiotics all have the  
24 same influence in that they would increase the  
25 digoxin concentration as opposed to decrease it?

A. I think that just generally





1

2 would be the case.

3

Q. Okay.

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THE COMMISSIONER: Increase it in  
5 the blood and decrease it in the tissue?

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THE WITNESS: Yes. So, you know,  
again, the magnitude here is something I think is  
a little difficult to ascertain at this sitting  
and if that kind of information were required I  
would like to go back and bring the references to  
you in a more precise manner.

11

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Q. All right. Finally, Doctor,  
you indicated yesterday that you reviewed Dr.  
Spielberg's evidence and Dr. Kauffman's report and  
that you found their assumptions and conclusions to  
be reasonable, is that correct?

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A. Not all. No, no, I found  
their assumptions - no, don't put me on record that  
way, please. I found that in general Dr. Kauffman's  
report, there were assumptions and conclusions that  
I was generally in concurrence with.

20

21

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Q. Yes.

A. With Dr. Spielberg's report  
there were some aspects of that that I disagreed with  
but I think it is important in the context I believe  
you are referring to to indicate that the pharmaco-  
kinetic analysis that they both presented I thought





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were very competent and I agreed in general with their conclusions.

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Q. You also indicated yesterday that you weren't certain that if you went through the same procedure of trying to estimate time and dose that you would bring any further understanding to these proceedings. Can you tell me what you meant by that?

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A. Well, only to indicate that I believe the assumptions they made were valid, that the restrictions on the interpretation they both made were valid, that the conclusions they reached regarding the potential minimum and maximum amounts of drug that might have been required to produce the levels in specific patients were of the order of magnitude that I would have agreed with and on that basis I didn't believe it was necessary to go through the same mathematical exercise. If you want to, I will bring a little computer down and we can run it off. But I do think that it was a replication of the same information.

21

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Q. Well, I take it then that in going through the exercise though all one can really achieve are possible ranges?

A. Possible ranges and a set of





1  
2 conclusions perhaps as to what concentration of drug  
3 could have been achieved in a rather fixed scenario,  
4 that is, making assumptions about the time the  
5 drug was given, making assumptions about the time  
6 the sample was taken in the patient and making  
7 assumptions about the degree of absorption of a  
8 given drug.

9                   These are all variables, as you  
10 have heard I am sure, and I thought that under the  
11 circumstances they both presented in as comprehensive  
12 a manner as possible, given the fact that hard data  
13 is actually lacking.

14                   Q.       Well, given the fact that  
15 it is lacking, is it not really an academic exercise  
16 in which one uses their best judgment to come up  
17 with the best assumptions they can and conclusions  
18 flowing from it as opposed to a precise exercise  
19 where one could pin a point with any degree of  
20 accuracy the exact time or dose?

21                   A.       Horrors! Do I hear you say  
22 that ...

23                   THE COMMISSIONER: Medicine is not  
24 an exact science?

25                   THE WITNESS: No, not medicine but  
the use of the mind to define this problem is academic.





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You did say that?

3

Q. Yes, I did.

4

A. Academic in that context is  
a very pejorative implication.

5

Q. It wasn't meant to --

6

A. I know you didn't mean to  
offend me but I am too old to get offended. I don't  
know if it is so academic. I think it gives us some  
sense of the boundaries within which we can reasonably  
approach this problem. That's really why, I don't  
think it should be discarded out of hand.

11

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Q. Yes.

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this patient.

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Now, one can go back and say, well,





1  
2 how was that achieved, and perhaps it does help you  
3 in your thinking as you go along with this investi-  
4 gation. But to say that it is a precise definition  
5 of what actually occurred I agree with you it would  
6 be erroneous.

7 MS. FORSTER: Thank you very much.

8 THE COMMISSIONER: Ms. Cecchetto?

9 MS. CECCHETTO: Thank you.

10 THE COMMISSIONER: Perhaps it might  
11 be a good time to take another poll. Ms. Cecchetto  
12 how long do you think you will be?

13 MS. CECCHETTO: About 10 or 15  
14 minutes, Mr. Commissioner.

15 THE COMMISSIONER: Yes, all right.  
16 Well then, we will lead into that, Mr. Roland,  
17 how long do you think you will be?

18 MR. ROLAND: 15 minutes, sir.

19 THE COMMISSIONER: I guess, Miss  
20 Chown, are you next, how long will you be?

21 MS. CHOWN: I will be about five or  
22 ten minutes.

23 THE COMMISSIONER: Mr. Brown? I don't  
24 know if I am going the right way, it has been so  
25 long since we have been at this.

MR. YOUNG: I think it is up to me, Mr.  
Commissioner. I have no questions for this witness.

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THE COMMISSIONER: Ms. McIntyre?

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MS. MCINTYRE: 15 minutes, Mr.

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Commissioner.

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MR. KNAZAN. I will be ten minutes,

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sir.

7

THE COMMISSIONER: Mr. Olah?

8

MR. OLAH: I will be about 15 minutes,

9

Mr. Commissioner.

10

THE COMMISSIONER: That just leaves

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the parents. It is unlikely you will be reached.

12

I have another meeting at the Court of Appeal and I

13

don't know whether they will miss me, but that may

14

be one more reason I should be sure to be there,

15

at 4:00 this afternoon. I do not think we will get

16

to the parents before tomorrow. I take it no parent

17

intends to be longer than half an hour, or does he?

18

MR. LABOW: At this point, Mr.

19

Commissioner, I might be a little longer than half

20

an hour.

21

THE COMMISSIONER: What about you,

22

Mr. Shinehoft?

23

MR. SHINEHOFT: I expect to be maybe

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ten minutes at the most.

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THE COMMISSIONER: All right, thank

you . Then, Ms.Cecchetto, we have cut into your





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time.

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CROSS-EXAMINATION BY MS. CECCHETTO:

4

Q. Dr. Mirkin, my name is

5

Lucy Cecchetto and I appear on behalf of the

6

Attorney General and several others. I am going to

7

ask you about medication error. It has been a

8

subject that has been put to a number of witnesses.

9

We have heard a great deal about the frequency of

10

medication errors in hospitals and a number of

11

doctors have opined about the frequency. Can you

12

tell me, Doctor, notwithstanding that medication

13

errors occur, in your experience is it very often that

14

these medication errors result in death?

A. I would say the answer to that

15

is no.

16

Q. Doctor, with respect to medica-

17

tion error would you expect to see the medication

18

error, absent some problem with a particular drug

19

on a ward, would you expect to see such error clustered

to a single ward?

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A. That of course would depend

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on the system for distribution of the drug in that

22

ward. For example, as you are well aware, in the

23

intensive care unit, particularly in the pediatric

24

unit, relatively small amounts of drugs have to be taken

25





1  
2 up out of an ampule into a syringe and it would not  
3 surprise me to see a large number of medication errors  
4 occur in that particular ward relative to other  
5 wards in the university. Probably a large number of  
6 medication errors go unreported, as you might imagine,  
7 and I can explain the reasons for that, if you like.

8 Q. I think we do accept that a  
9 great many people do not realize that they have  
10 made a medication error and it goes unreported.  
11 If you would like to explain the reason for it,  
12 Doctor --

13 A. I don't want to cut into your  
14 time.

15 Q. Would you expect in a cardiac  
16 ward to see a clustering of errors with respect  
17 to digoxin restricted to a single nursing team  
18 in a single time frame?

19 A. That, with all the contingencies,  
20 would be a very unusual event. While no one can  
21 answer that with certainty, perhaps someone in that  
22 event has very poor vision and cannot see what  
23 they are taking up in a syringe, but the answer  
24 of course is that that is unusual and would not  
25 be expected.

Q. Doctor, yesterday when you were





1  
2 going through your categorization of the deaths  
3 you dealt with four children who had apparently  
4 received digoxin and none was prescribed for them.  
5 That was the Lombardo child, the Belanger child,  
6 the Hines child and the Cook child. I am going to  
7 leave Cook out of the picture for the moment.  
8 In respect of medication error and the theory of  
9 medication error at Volume 71 of the transcript,  
10 page 5661, Doctor, Ms. Cronk when she was examining  
11 Dr. Kauffman put to him the theory espoused by Dr.  
12 Spielberg. Dr. Spielberg basically indicated he  
13 was of the view that there was a possibility that  
14 the babies Belanger, Lombardo and Hines had all  
15 received digoxin in error. She also put to Dr.  
16 Kauffman the view that Dr. MacLeod had expressed which  
17 was basically that he found the probability of all  
18 three of them having received digoxin in error to be  
19 more remote. He might have accepted one and possibly  
20 two but he found it more remote with respect to all  
21 three. Can you give us your opinion on what the  
22 probability would be that all three of these children  
23 received digoxin in error?

24 A. I think that is a large number  
25 of medication errors to postulate. Of course, one  
would question, did these occur in close proximity --





1  
2 these alleged medication errors occur in close  
3 proximity to one another from a temporal perspective.  
4 Were they one day after the next? Were they three  
5 events occurring over a year and a half? If they  
6 are then one could say that this might not be  
7 such an exceptional phenomenon.

8 But I would like, I think, to be  
9 more productive in a sense. If one examines, getting  
10 back to the previous questioner, how much might have  
11 been given to each of these children, based on the  
12 theoretical calculation of previous consultants,  
13 of Spielberg or of Kauffman, then it seems to me  
14 you could come up with an interesting analysis of  
15 the likelihood of medication error. For example,  
16 it is very reasonable that a medication error can  
17 occur when one is drawing up relatively small amounts  
18 of digitalis solution in a syringe. Instead of  
19 drawing up .05 you draw up .1 or .06. Those things  
20 very likely have happened, will happen, but the question  
21 comes up, if one had to give a much larger amount of  
22 that compound to account for the concentration that  
23 may have been achieved in this patient, then you are  
24 talking about someone drawing up huge amounts of this  
25 compound and that is not feasible, in my mind. It is  
not consistent with a medication error. A medication





1  
2 error I think is generally made on a smaller  
3 volume. I hope you will follow my convoluted  
4 reasoning. I would not expect error to be made  
5 where we are postulating large amounts of drug  
6 administration.

7 Q. I understand what you are say-  
8 ing, but with respect to the three children that I  
9 posited, Lombardo, Belanger and Hines, they were  
10 not prescribed digoxin so the fact that they received  
11 it was the error. Unfortunately, with respect to  
12 Lombardo and Belanger, all we have are the exhumed  
samples and there are problems in extrapolating that.

13 A. May I interrupt you.  
14 Okay, in my verbosity I forgot the question. The  
15 key issue is no. With the patient not being pre-  
16 scribed the drug -- I am sorry about that -- I would  
17 agree with you that it would be very unlikely that  
18 they received that drug as a medication error.  
I tend to preclude that as a realistic possibility.

19 Q. Now, Doctor, yesterday you  
20 testified that with respect to Cook, Miller and  
21 Pacsai it was your view that they died of digoxin  
22 intoxication and you further testified at Volume 87,  
23 page 8909 for my friends that in your view they  
24 died as a result of a substantial overdose --  
25





1  
2 or your words were an overdose in the toxic order  
3 of magnitude.

4 With respect to Cook, Doctor, would  
5 this not involve two errors, in view of the fact  
6 that Cook was not prescribed digoxin and, secondly,  
7 not only would he have to be given a dose that was  
8 not prescribed but he would have to be given a toxic  
9 dose.

10 A. Yes, certainly if you are --  
11 accepting the second postulate that the administra-  
12 tion was in error.

13 Q. Doctor, there has been a  
14 scenario put to a number of witnesses with respect  
15 to Baby Justin Cook. If the doctor could be provided  
16 with Justin Cook's chart, it is Exhibit 116, I am  
17 going to refer you to page 29. First of all, Doctor,  
18 before I get into the area, I would like to show you --  
19 we have had entered as exhibits certain vials and  
20 it is my understanding that the medication was in the  
21 same type of vial at the pertinent time. The vial  
22 that I am interested in is a vial of inderal,  
23 propranolol and a vial of digoxin, that is the adult  
24 compound. This is the pediatric digoxin and this is  
25 the adult ampule.

A. Okay, thank you.





1  
2 THE COMMISSIONER: Was there a  
3 question and answer?

4 MS. CECCHETTO: No, I was just show-  
5 ing him the vials.

6 THE WITNESS: I said thank you.

7 Q. Doctor, the scenario that has  
8 been posited has been that perhaps through error  
9 Justin Cook received digoxin instead of propranolol.  
10 If you turn to page 29 of the chart it is indicated  
11 there under note of Nurse Nelles that at approximately  
12 3:45 the baby began to experience difficulty and then  
13 the note continues and that propranolol was  
14 administered on the arrival of Dr. Kantak and  
15 subsequently a second dose of propranolol was  
16 administered at approximately 3:55.

17 If you turn to page 30 on that same  
18 chart it will give you the volume of propranolol  
19 or inderal that was administered and they were  
20 .4 millilitres and .2 millilitres for a total of  
21 .6 millilitres of propranolol.

22 Now, Doctor, you have the concentra-  
23 tions that were in the pediatric file of digoxin  
24 and that is .05 milligrams in one millilitre in the  
25 adult vial which is .25 milligrams in one millilitre.  
Given those concentrations and in view of the fact





1  
2 that the series of events that occurred here were  
3 that the child began to experience difficulties  
4 at 3:45, it went into cardiac arrest at 4:20, a  
5 code 25 was called. At 4:30 there was a sample taken  
6 which rendered a 72 blood reading in serum and  
7 at 4:56 the arrest stopped and the child was pro-  
8 nounced dead. Given those factors and given those  
9 readings in fresh tissues that were found, that the  
10 child had an 11.66 reading in the ventricular  
11 myocardium, in your view, Doctor, could a substitution  
12 of digoxin for propranolol have accounted for the  
13 serum and tissue level?

13 A. When you talk about a substitu-  
14 tion, the presumption is that 0.6 mls. of either  
15 the pediatric or adult digoxin might have been  
16 administered.

16 Q. .6 I have, Doctor.

17 A. I said 0.6. It is the same  
18 as yours.

19 Q. All right.

20 A. If one calculates it out,  
21 and I am sure others have, if you take the pediatric  
22 digoxin dose which is .05 milligrams per millilitre,  
23 that is equivalent to a total of 50 micrograms in  
24 one mil. and you take .6 of that, that is 30 micrograms.  
25





L: 2  
DM:  
yk 3

1  
2 Presume 30 micrograms were givento this child; this  
3 child weighed 5.4 kilograms that is 6 point, roughly  
4 6 micrograms per kilogram to this patient, which  
5 would now accomplish or achieve that particular  
6 blood level when given to that patient. So we  
7 must reject the possibility that .6 of the pediatric  
8 dose was given.

9 Let's examine the possibility that  
10 .6 of the adult dose was given. That in my  
11 calculations would be 150 micrograms from that  
12 dosage, that type of ampule and that comes out to  
13 about 30 micrograms per kilogram, which certainly  
14 is in excess of what we would want to give a  
15 child, but likewise produces problems when we look  
16 here at extraordinarily high blood levels, presuming  
17 that the blood level was obtained how many hours  
18 after the alleged dosage.

19 Q. Well right here the dosages  
20 would have been given between 3:45 and 4:20 because  
21 the blood level was taken at 4:20.

22 THE COMMISSIONER: No, no, 3:45 and  
23 3:55.

24 MS. CECCHETTO: Yes 3:45 - 3:55.

25 Q. Yes, 3:45 and 3:55, Doctor,  
and the blood level was at 4:30.





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A. So we are talking about 45 minutes, or something of that order?

Q. Yes.

A. Yes, I think it is unlikely that you will achieve that.

Q. What about Doctor, aside from the blood levels, what about the levels in the tissue, are you prepared to --

A. Well I want to, as I have throughout this testimony, place minimal significance on the quantitative use of that data. I would think that the qualitative information may be helpful considering the fact that this patient was not supposed to be on the drug; considering the fact that this patient somehow received it. I think it is reasonable to assume that the amounts we did find could not have been produced by this single dose of this magnitude. Or I should say would have been unlikely to have been produced by that.

Q. And Doctor I showed you the vial of Inderal and the vials of the pediatric and adult concentration of digoxin. The Inderal is in the brown vial and both the pediatric and the adult concentrations of digoxin are in clear coloured vials. Can you give me your opinion on what the likelihood is





1  
2 of confusing those two vials?

3 A. I guess it is possible someone  
4 is colour blind, but it is difficult I think.

5 Q. How, Doctor, if I could put  
6 to you a question that I put to Dr. Kauffman. We  
7 all understand that medication errors occur, but  
8 how would you feel if you had the power to continue  
9 or discontinue the employment of a person who made  
10 a medication error such as the one suggested in  
11 Justin Cook's case, erroneously administered digoxin  
12 for propranolol in view of the fact that the vials  
are different colours and of different sizes?

13 A. Well I certainly would not  
14 categorically dismiss them, I think I would investigate  
15 the case.

16 THE COMMISSIONER: How are you now?

17 MS. CECCHETTI: I think that  
18 concludes my cross-examination.

19 THE COMMISSIONER: Yes, all right,  
20 thank you. Then we will rise until 2:30.

21 --- Luncheon Recess.  
22 -----  
23  
24  
25





AA: 1  
DM:  
yk 2

--- Upon Resuming at 2:30 p.m.

THE COMMISSIONER: Mr. Roland.

MR. ROLAND: Thank you, Mr.

Commissioner.

CROSS-EXAMINATION BY MR. ROLAND:

Q. Dr. Mirkin, my name is Ian Roland and I act for the Hospital for Sick Children. I just have a few questions for you about your work.

First of all, as I understand your evidence as it stands today, you consider at least I think by my count eight babies to be in one or category/another of suspicious deaths as a result of digoxin intoxication; and the babies you gave us the other day and I think you have added, you have taken out and I think you added back in today Estrella, Janice Estrella; they are Lombardo, Belanger, Estrella, Hines, Pacsai, Inwood, Cook and Miller, and we will talk about David Taylor in a minute, but apart from him those are the babies you have told us that you have an index of suspicion about as far as digoxin intoxication is concerned in their deaths. I note from all of those that there is toxicological information either ante mortem, certainly with respect to Cook and with respect to the others post mortem information, either serum or

25





1  
AA22 tissue levels. I take it those play a substantial  
3 role, as you have said, in your determination to  
4 place those babies in the one of three categories  
5 of suspicion that you have given us?

6 A. Well they do play some role,  
7 but it is also important to recognize that the fact  
8 that some of these babies also had evidence that  
9 was consistent with digitalis intoxication, in  
10 addition to the fact that toxicological information was  
11 present.

12 Q. Well, with respect to those  
13 eight babies that I have named on your scoring.

14 A. Yes.

15 Q. Dealing with the indicators  
16 at least in the charts and the information that you  
17 had during the clinical history, you scored all of  
18 them zero except for Kevin Pacsai and Janice  
19 Estrella. So I presume that the toxicological  
20 information which you didn't have, or you didn't  
21 use in doing that scoring, is very significant in  
22 the babies other than Janice Estrella and Kevin  
23 Pacsai?

24 A. Yes because - I will accept  
25 what you say.

26 Q. And with respect to Janice  
27 Estrella, which you score as a 9.3, I take it it is





1  
2 clear that that is because, and we all recognize  
3 in the chart, that her digoxin level was substantially  
4 elevated during life, although coming down before  
5 her death.

6 A. No, it has got to go beyond  
7 the mere presence of the blood levels. You see  
8 you are inferring as far as Estrella is concerned  
9 that that was the only basis on which that high  
10 score was based. In ESTrella, if we can look at  
11 that for a moment, you will see that there was,  
12 in our opinion at least, substantial clinical  
13 evidence that this patient was having a significant  
14 effect that could have been attributed to the  
15 digitalis. So to be more precise about your  
16 evaluation I would say that in-Estrella was based  
17 on both pieces of information, that is the clinical  
18 findings, electrocardiographic, and the toxicologic  
19 information.

20 Q. And the toxicological  
21 information very substantially you will agree  
22 confirmed the clinical findings that it appeared to  
23 be related to digoxin?

24 A. As much as it could, yes.

25 Q. And with respect to Kevin  
Pacsai, I gather when you rate Kevin Pacsai as a 9.1





1  
2 you rely, if not exclusively, to a substantial degree,  
3 on the fact that there was a greater than 10 reading,  
4 a serum level reading for digoxin in the hours  
5 prior to his death and that is one of the things,  
6 and a very significant thing that leads you to rate  
7 that as a 9.1.

8 A. Do you want me to answer  
9 you, or do you want to tell me what I said?

10 Q. I want you to agree or  
11 disagree with what I say.

12 A. I am not going to agree with  
13 what you said, that is not how this scoring was  
14 achieved and I think you are aware of that. I think  
15 that to infer that the diagnosis on Pacsai was  
16 achieved primarily because of the high blood level  
17 is not a correct assessment. What we had here  
18 was clinical evidence in our opinion that strongly  
19 was consistent with digitalis intoxication. We  
20 did have, as you suggest, evidence, toxicologic  
21 data or pharmacologic evidence that this patient  
22 had a high digoxin level. Now that in itself  
23 did not make the diagnosis for us, I really want  
24 to emphasize that if I may,

25 Q. Well let's talk about it  
temporally. I gather the indicators other than the





/rc  
AA5

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digoxin level, a serum level of greater than 10 occurs concurrently with that reading?

A. Yes, but as you are well aware and I am sure --

Q. You are not talking about some other time?

A. No I am talking about my notes at least, we have on 3.11 at 1530, I hope that is correct, yes, we have an EKG a little after 1530 which shows a response which can be attributed to digitalis. There is a lengthening of the PR interval; there is a slowing of the heart and the question of digitalis intoxication is raised. Now at the same time, and though I take it that blood level of greater than 10 was obtained on March 12th, of that day, is that correct?

Q. Yes. Around six o'clock or something.

A. Now if I were on the ward let us say I might have made that diagnosis of digitalis intoxication from the electrocardiogram alone without the assistance of the high blood levels. The blood level was confirmatory and I just want to put it in perspective, I don't want to diminish the significance of that information.





Mirkin  
cr.ex. (Roland)

AA6

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Q. Which information, the blood level?

A. The blood level. Also though I don't want to leave you with the sense that that is the only basis upon which this decision is made, okay.

Q. Is it fair to say that the blood level as you say gives you some confidence and a substantial degree of confidence in scoring this as 9.1, you might not have scored it as high but for the blood level?

A. Oh, I see. No I think that this probably would have been scored high in the area of 9, perhaps as high as that, even in the absence of that information.

Q. And I understand and you have told us, and the chart discloses, that there was a suspicion at that time on the 11th when the EKG changes were noted that there was a suspicion of digoxin toxicity and an order to hold digoxin and that is the proper clinical response to that kind of information?

A. Correct.

Q. And there was no indication of any digoxin being therapeutically administered





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Mirkin  
cr.ex. (Roland)

AA7

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after that?

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A. My record shows no drug

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being given after identification of the question,

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of the problem, on March 11.

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Q. Now, apart from those

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then that of the other six babies had any indication

4

of digoxin toxicity, that is, as you examined them

5

you scored all of the other babies as zero and I

6

gather then there was unanimity in your team that

7

looking at the clinical records and setting aside

8

the toxicology results that they didn't disclose any

9

signs or indicators of digoxin toxicity; no evidence  
of it.

10

A. That is correct, though with

11

the exception of Taylor, of course.

12

Q. Yes. Well, we will talk about

13

Taylor in a minute because Taylor is a little odd.

14

You come to quite a different conclusion than in all

15

the others without any toxicology. But we will talk

16

about that in a minute. I am just talking about the

17

other six. So, you really relied, we have agreed,

18

with respect to the other six, when you come to your

19

index of suspicion that digoxin played a role in the

death of those other six really from the toxicological  
information.

20

A. I think that is correct.

21

Q. Then when we go to the babies,

22

and let's still set Taylor aside for the moment,

23

the babies in which you can give as a relatively

24

25

BB  
/PS





1  
2 high score, certainly over 7, but you aren't  
3 suspicious about digoxin, you aren't substantially  
4 suspicious about digoxin playing a role in the death  
5 of those babies we have Brian Gage, and I gather  
6 with respect to Brian Gage what you say is that  
7 some time during the course of his clinical experience  
8 there was a high reading or there was some indication  
9 of digoxin toxicity but you don't attribute the  
10 digoxin as playing a role in his death and I see  
11 from the chart we have in evidence that there was,  
12 among other things with respect to Brian Gage, an  
13 indication of a 3.5 blood serum level taken the day  
14 before he died and I gather that was a factor in,  
15 although it is not a substantially elevated blood  
16 level, it is a blood level that is beyond the  
17 normal therapeutic range and that would be a  
18 consideration for your team in scoring Brian Gage  
19 as high as 7.2. Is that fair?

18 A. I think that's fair.

19 Q. Yes. And I gather we have it  
20 that the last therapeutic dose for Brian Gage was  
21 about 19 hours before he died and it is fair to  
22 say that one would expect that this serum level would  
23 come down below 3.5 in the 19 hour interval between  
24 the last therapeutic dose and the time he died.  
25





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A. Why do you say that?

3

Q. Well, because it is excreted,

4

in the normal course it is excreted from the body

5

and the blood level I gather tends to fall over time.

6

A. That's true.

7

Q. That's what you would normally

8

expect.

9

A. Normally expect.

10

Q. Yes.

11

A. Now, was this patient normal?

12

Q. Well, was he normal. Would

you expect it with this patient from your review of  
the chart?

13

A. No.

14

Q. You wouldn't.

15

A. I think it is important to

16

recognize that this patient had a creatinine of

17

2.2.

18

Q. Yes.

19

A. And as you know by now, that

20

is generally associated with some degree of renal  
malfunction.

21

Q. Yes.

22

A. Renal insufficiency, as one

23

might describe it.

24

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Q. Yes.

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A. So that the proposition you

4

put to me that the drug is going to be cleared at

5

a normal rate might not hold in this subject. In

6

fact, it probably does not hold in this subject

7

because an infant of this age with normal kidney

8

function would be expected to have a creatinine,

9

serum creatinine in the range of 0.3 to 4.

10

Q. Yes.

11

A. So this to me I infer that this

12

patient is having difficulty clearing drug from the

13

body, therefore, that dose might have not been

14

cleared adequately, inferring perhaps that even normal

15

amounts of digoxin that were given to the baby could

16

have accumulated during the time between 9:11 and

17

9:24 or 9:17, I should say, when the creatinine is

recorded and 9:24, the time of the baby's death.

Do I make myself clear?

18

Q. Yes. We have the 3.5 level

19

taken I think on the 24th.

20

A. Correct.

21

Q. And the baby died on the 25th.

22

A. Yes. So, you have the day

23

before, as you have indicated, a level which is in

24

a toxic range and therefore conceivably is compatible

25





1  
2 with a digitalis intoxication like picture.

3 Now, I thought you were asking me to  
4 agree with you that the dose, the last dose given  
5 to this time had been cleared normally and I would  
6 be unable to agree with that point when presented  
7 with these data that suggest some degree of renal  
8 impairment.

9 Q. Yes. And as you indicate  
10 the degree of renal impairment is shown some 7  
11 or 8 days prior to the baby's death.

12 A. It seems on the 17th. Now,  
13 if you have data, later data suggesting that the  
14 renal function was normal perhaps then that scenario  
15 has to be discarded.

16 Q. And I take it you would agree  
17 with me that although 3.5 is somewhat elevated from  
18 the therapeutic range, it is not something that is  
19 really in the range you have to worry about it  
20 being terribly serious, it is elevated and you want  
21 to bring it down, but you don't have to get too  
22 concerned about it at that level.

23 A. I think that is a fair  
24 assessment, I would accept that, certainly.

25 Q. Now, the next baby, Richard  
McKeil, your team puts it at 8.1. He had a serum





1  
2 level of 4.7 on October 14th. I take it that again  
3 was a significant fact in rating him at 8.1, that it  
4 showed an ante mortem level that was again beyond  
5 the therapeutic range.

6  
7 A. Well, it was a factor. I  
8 think it is important also to recognize that this  
9 patient had many signs of digitalis intoxication;  
10 emesis, had cardiac arrhythmias and this is a pattern  
11 that quite -- inverted T-waves in the electrocardio-  
12 gram. This is a pattern very consistent with  
13 intoxication. So, not only is it the blood level that  
14 is a determinant here, it is also the clinical find-  
15 ings that lead us to this conclusion.

16 Q. With respect to the ECG readings  
17 in Richard McKeil we have had it in evidence from  
18 Dr. Rowe that although the electrocardiogram readings  
19 may be compatible with a digoxin effect that they are  
20 not characteristic of digoxin toxicity. Did your  
21 team agree with that?

22 A. Well, we had signs here of  
23 digitalis effect, as you know, which is not the same  
24 as digitalis intoxication. But I think the fact that  
25 this patient presented with slightly irregular pulse  
and also on the 13th was showing premature apical  
beats, I'm not sure how a cardiologist would not





1  
2 interpret that as an arrhythmia.

3 I don't know whether we have  
4 electrocardiograms from that date, but I would be  
5 willing to hazard a guess anyone who would look at  
6 such an electrocardiogram would come up with the  
7 same conclusion as we did.

8 Q. Well, I can't read them, but  
9 I can tell you that as I have it, that Dr. Rowe  
10 said that the readings do not preclude digoxin  
11 toxicity all together but high levels of digoxin  
12 that are sufficient to cause the baby to die should  
13 have been reflected in a more important fashion  
14 on the ECG than they were.

15 A. Well, what does Dr. Rowe mean  
16 by important fashion, can you let me know? Is he  
17 a cardiologist? He's the pediatric cardiologist  
18 here?

19 Q. Yes, yes.

20 A. Well, why don't you have him  
21 write out what that means, I would appreciate it  
22 and I think you also ought to.

23 Q. You are not familiar with  
24 Dr. Rowe?

25 A. I have heard of him. He's  
Canadian? He's here, right?





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Q. He's here, yes.

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A. Yes, right, fine. I think that in my opinion I would have liked to have known his interpretation of PR interval, whether there were irregular beats, what the conduction velocity, a lot of data that can be derived from a man with his experience I am sure who knows that and could have put it down. Is there information on that in the record, do you know? It would be nice to know.

Q. I can give you a summary of what his evidence is. I don't know that his evidence answers your questions the way you pose them.

A. Well, if I may be of some assistance on this here. Our cardiologist in reviewing the electrocardiogram on October 14th, we don't know exactly when this was in relationship to the dose of digoxin that was withheld, the patient had a very significant change in the ST segment. Now, that's not indicative or diagnostic of digitalis intoxication, that would concur with Dr. Rowe.

Q. Yes.

A. I think that the arrhythmias that were reported in the chart, though I think are consistent with it and we don't have electrocardio-





1  
2 grams from the time that the patient was showing  
3 more severe signs of digitalis intoxication, at  
4 least what we presumed to be digitalis intoxication,  
5 and if those electrocardiograms are available, I  
6 think they would be very important in analyzing this  
7 case.

8 Q. All right. Let's turn, Doctor,  
9 to Real Gosselin. It is your code No. 29. You have  
10 rated this as a 7.1. Real Gosselin as well had an  
11 ante mortem serum level of 3.9 and I gather that  
12 is an indicator to your team that there is some  
13 perhaps digoxin toxicity at the low range, that it  
14 is again somewhat slightly over the therapeutic  
15 range.

16 A. Yes. Now, I think we shouldn't  
17 use the term slightly over a therapeutic range so  
18 lightly. What numbers are we assuming to be the  
19 therapeutic range in this patient or in this age of  
20 patient, I think that would be important to know.

21 Q. Well, I think we have heard  
22 1 to 2.5 I think is the sort of most common range  
23 that we have heard.

24 A. Okay. Now, if we are going  
25 to accept 2.5 as an upper range now, 3.9 is more  
than 50% above the upper range of normal.





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3 Q. Right. That is what I pre-  
4 sumed when you looked at that number, it is that  
5 number among other things that was a strong indicator  
6 for you to rate this baby at 7.1, that is all I am  
7 asking you.

8 A. Okay, fine, okay. I want  
9 to get as quantitative a statement as possible into  
10 the record, that's all.

11 Q. Yes, yes. You felt as well  
12 that this death was unexpected or unanticipated.

13 A. That is correct.

14 Q. And I gather from your evidence  
15 and in reviewing this chart, and I think you mentioned  
16 this in your evidence, that Dr. Freedom had written  
17 a letter in the chart to Dr. Miller at which he  
18 expressed the doubt that the demise of the baby could  
19 be explained truly on the basis of apnea secondary  
20 to the prostaglandin therapy. Do you remember that?

21 A. I don't recall saying that.

22 Q. Do you remember the letter in  
23 the chart, a notation of that?

24 A. I'm quite sure I didn't  
25 cite the letter.

Q. Well, let me tell you that the  
letter is in the chart and it was a subject of some





1  
2 substantial discussion when Dr. Freedom testified.  
3 Dr. Freedom is a pediatric cardiologist of some  
4 reknown as well. American, by the way, but  
5 working here at the Hospital for Sick Children.  
6 He said that when he wrote that letter on December  
7 18th he hadn't reviewed the chart and he said in the  
8 letter that he didn't have a good explanation for  
9 the sudden deterioration or the death of the child  
10 when he wrote in the letter, that's what he expressed  
11 in the letter, but the letter taught him a lesson to  
12 review the chart and when he went back afterwards and  
13 reviewed the chart and reviewed I think as well the  
14 post mortem he said he was embarrassed about writing  
15 that letter the way it was because in fact on  
16 reflection the child didn't have a good response  
17 to prostaglandin he thought and that the child's  
18 death and in the way the child died rather suddenly,  
19 deteriorated rather suddenly was due to the fact that  
20 there was a poor response to the prostaglandin and  
21 that the ductus closed or the prostaglandin didn't  
22 keep the ductus open.  
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Now, in light of that, and we agree I think that the death was sudden, sudden deterioration, but in light of that information, it was not unexpected that it would be a sudden deterioration.

If you accept Dr. Freedom's assessment of what happened, it would be a rather sudden deterioration in the infant's condition, would it not?

A. I am certainly willing to accept Dr. Freedom's interpretation of events. He was there. He had a clearer view of what was going on, and one has to accept that.

THE COMMISSIONER: I do not think he was there, that is the problem. If he had been there, perhaps we would not have had this problem. He wrote a report based on what he had heard, then he gave evidence here. He then examined the charts and thought differently. So it is not a question of his being there. He has no better idea about it than you have - I may not be quite right about that, he may have spoken to more people than you have - but his evidence is based upon the chart itself and based upon what he now believes was the effect of this drug, this prostaglandin, and whether it was working or was not, and that he gets from the





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chart. In fact, I think he got a somewhat different story from the attending clinician.

THE WITNESS: I think one of the points, I do now recall reading a letter here, not Dr. Freedom's letter but the letter from Dr. Stephens which is very interesting. It is the discharge report and it does indicate that this patient did have a positive response to the prostaglandin. That is on page 21 of the chart.

You see that report - the discharge report - on the bottom, five lines from the bottom, says "prostaglandin infusion, child was started on prostaglandin infusion. Accepted protocol dose." The child did well during the day but had two brief episodes of apnea. The child was given Lasix and the arterial blood gases and electrolytes taken at that time were within completely normal limits. The child did well until the 18th, at 2:25, and had bradycardia and died.

But the point is that this child did respond to prostaglandin apparently from this clinical -- whether it was a sustained response, I don't know, but --

MR. ROLAND: Q . Let us not debate that, doctor. Let us accept Dr. Freedom's evidence





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CC3 2 for the moment and say that, in his view, in reviewing  
3 this, and I think he may have participated in the  
4 autopsy - I'm not sure, but let us accept his  
5 clinical opinion that the child had an inadequate  
6 response to prostaglandin, whether it was at the  
7 outset or whether it was an inadequate sustained  
8 response, let us assume that. All I am asking you  
9 is, is that so, if we accept Dr. Freedom's evidence  
10 on that point, then the terminal events will be  
fairly precipitous and dramatic, will they not?

11 A. One would expect that, yes.

12 Q. So, if one thought that there  
13 was a good response to the prostaglandin, one  
14 would not have anticipated the death. If one  
15 recognizes that there was not a good response to  
16 the prostaglandin, one would anticipate a fast  
demise. Is that correct?

17 A. I think that probably would  
18 follow.

19 Q. That is the only point I  
20 wanted to make.

21 Turning to David Taylor, doctor,  
22 David Taylor, I quite frankly have a hard time  
23 understanding because you do not have any toxicology  
24 on David Taylor and every baby that we have looked  
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at that has a high score or is a baby in which you say you have a strong suspicion or index of suspicion died of digoxin overdose has some toxicological information associated with it, whether it is serum levels or post mortem levels. If you look at every one of the babies that you rate over 7, or every one of the babies that you say is a suspicious death, they all have some toxicological information except for David Taylor.

MR. LAMEK: Excuse me, Mr. Commissioner, my recollection is that Woodcock too was included in Dr. Mirkin's list yesterday in that zero score of no toxicological information.

THE WITNESS: That is correct.

MR. ROLAND: Q. So Woodcock is the other one. You have a zero score, though, with Woodcock and a 9 score with Taylor and, yet, they both demonstrate much the same arrhythmias. There may be some debate about whether it is near enough to be a terminal event but they both demonstrate arrhythmias. I gather the fact that you score Woodcock as a zero even though there are some arrhythmias means that those kinds of arrhythmias by themselves are not taken, at least in Woodcock's case, to be indicative of digoxin intoxication during





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A. I think we felt that the arrhythmias presented in Taylor's situation were very strongly consistent with the diagnosis of dig. intoxication. That was our interpretation. You correctly note this was concluded in the absence of toxicological proof, that this was induced --

Q. Or support, even. Whether it is proof - but there is no support at all.

A. Proof, really. If the drug is present, at least we can make an inference that it is indeed acting if we demonstrate its presence. It was never demonstrated. This was never done. Studies were not performed. So there is no data to support the presence of the drug. This is an inferential conclusion. The inference here is that these findings are consistent with digitalis intoxication and, if one were to ask me my best judgment as to whether the death of this patient could have been associated with digitalis intoxication, assuming that these arrhythmias are indeed induced by digitalis, then I would say, yes, that this death could have been induced by that, and that is essentially all that one can say.

Q. You go at it from the other end, though. You look at the arrhythmias and





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you assume that they are indicative of digitalis intoxication rather than saying there is digitalis intoxication and the arrhythmias are a response to them. You use the arrhythmias, I take it, in Taylor to come to the conclusion that there is digitalis intoxication?

A. Yes, I think that is correct. You are suggesting that, in other circumstances, we have made a decision based on toxicological data and come backwards.

Q. I compare Woodcock to Taylor, and you have much the same arrhythmias but you don't use those arrhythmias to conclude any digitalis intoxication.

A. Was Woodcock not one that we --

Q. Woodcock scored a zero.

MR. OLAH: In yesterday's evidence, you will recall Woodcock was in the same category as Taylor of suspicious death. That was the doctor's evidence.

MR. ROLAND: Q. You scored a zero during life for Woodcock. During its clinical course, you scored a zero. Those arrhythmias occurred during its clinical course and your team





1  
CC7 2 scored it as a zero. Therefore, you did not put  
3 any significance on those arrhythmias in relating  
4 them to digitalis intoxication. Much the same  
5 arrhythmias you used in Taylor to come to an  
6 opposite conclusion; that is, that they were indica-  
7 tive of digitalis intoxication.

8 I am having a hard time under-  
9 standing that except for what may have been an  
10 explanation this morning; that Taylor was on digoxin  
11 and Woodcock was not. Is that the only difference?

12 A. I think that that is a  
13 reasonable conclusion.

14 Q. And on page 124 of your  
15 report --

16 A. What patient does this refer  
17 to?

18 Q. You told us that Dr. O'Dea  
19 prepared this. It is Taylor, Chart Code 1, Dr. O'Dea,  
20 and you have told us, of course, that he did this  
21 at the outset before the meeting, but he appeared  
22 to look at the EKGs --

23 A. No, Dr. Moller did.

24 Q. Sorry, was it Dr. Moller?

25 A. Yes. We put this into the  
chart.





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Q. He looked at the EKGs and he says, as I read it - you correct me if I'm wrong - that the EKG changes could be due to digitalis, however, they could also be due to the condition of the patient.

A. I think I pointed that out when this patient was discussed this morning.

Q. So, really, the only way in which you arrive at a 9 in Taylor, I gather, rather than a zero, as you did in Woodcock, in deciding whether there was digoxin intoxication during life is the fact that Taylor was on digoxin and Woodcock was not?

A. I think that is certainly an important component in these two cases, but the particular type of phenomenon that we saw in Taylor, one might argue is even more compatible with the electrocardiographic changes perhaps that one finds in digitalis intoxication, and to say that there were very significant differences between Woodcock and Taylor in their electrocardiographic irregularities, I would have to go through that again.

One of the problems that confronts us in my completely accepting the position you try to put me into is that we do not have large numbers





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CC9 2 of electrocardiographic tracings in these cases that  
3 we can compare with one another, and that is a  
4 problem. But I think, just to get the record  
5 straight here, I would say that the fact that one  
6 of these patients, that is, Taylor, had been  
7 receiving digitalis and had shown digitalis effects,  
8 so to speak, was an important piece of information  
9 leading us to that high score.

10 Q. An effect, really, which  
11 could be digitalis; a digitalis effect or could equally  
12 be an effect from his clinical condition.

13 A. I would not put "equal" to  
14 it. The truth of the matter is that probably no  
15 one knows. But, in our opinion, we felt that this  
16 was more likely due to a drug-induced effect.

17 Q. I have a hard time with  
18 Dr. Moller's wording. He reviewed the EKGs. He  
19 is the one that did the review, and his wording,  
20 you told us, transcribed on page 124, does not put  
21 it nearly as high as you do.  
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Q. He is the one that did,  
I take it, give that information to your committee,  
he interprets it, and his interpretation as we have  
it on page 124 has it, has a quite different  
emphasis than the emphasis you are giving to us today.

A. What do you read in it?

Q. Well, if he is the source  
of your information, I am reading from your source  
and your chart, Code No. 1, and as I understand it  
you have told us that was the transcribed information  
from Dr. Miller's review of the EKG and it doesn't  
give to me the emphasis that you now give. You  
tell us he is the source of information for your  
committee, or your team.

A. Why doesn't this give you the--

Q. Well, you say it is not even  
equal, and he says:

"Conclusion: digitoxin intoxication  
cannot be excluded."

And that really is I think fairly a much lower  
index --

A. Where do you see that, what  
page?

Q. I am sorry, I am looking at  
your chart No. 1.





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A. You are looking at the wrong  
information, I would suggest.

4

Q. I see. I thought you told us  
that this information was transcribed --

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A. Let me tell you what is.

7

Q. All right.

7

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A. What is -- that Dr.

8

9

Miller's comments are on this appendix

9

there of David Taylor. Now as I think went into

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testimony this document has some typos in it and

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does need to be proofread more completely. But

12

let us accept the information here at its face

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value. The EKG's that he had available showed

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rhythm changes compatible with digitalis intoxication;

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showed changes in the ST segment; showed a 2 to 1

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block. I think any cardiologist seeing that would

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find that compatible with digitalis intoxication.

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Considering this patient's disease, I also would agree

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with you that there are some of these findings that

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are certainly compatible with the disease process,

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so I don't want to be too obstinate in that.

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The real issue is what kind of

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weighting is given to the disease versus the drug

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induced possibility, I think that is what you and I

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2 probably are trying to resolve. We felt that this  
3 was more likely due to a drug induced phenomenon  
4 than from the intrinsic process. I certainly will go  
5 on record saying that there can be individual dif-  
6 ferences of opinion, and that Dr. Rowe's judgment  
7 is going to be as valid as mine and I think that should  
8 go into the record.

9 Q. Just so I understand, before  
10 we leave David Taylor; looking at Exhibit 133 in your  
11 Code No. 1, David Taylor, I am sorry, 313.

12 A. I'm sorry, I missed you on  
13 that.

14 Q. David Taylor it is your chart  
15 Code No. 1 and it is the last page of that.

16 A. Yes.

17 Q. And that is, it appears to be  
18 the writing of Dr. O'Dea.

19 A. That is correct.

20 Q. And it appears he reviewed  
21 the EKG. Now, is that -- or did he get that informa-  
22 tion out of the chart, or where is that information,  
23 where did that information come from?

24 A. I don't know. Occasionally  
25 there were EKG's in the chart, there may have been  
data from your staff at the Toronto Children's Hospital





1  
2 staff, or -- I do want to remind you that we all  
3 are physicians and we do know how to read these  
4 things and this may have been his interpretation, too.

5 Q. All right, that is fair  
6 enough. I misunderstood you then, I gather, when  
7 I thought this was a transcription of Dr. Miller's.

8 A. Oh, I'm sorry if I did say  
9 that.

10 Q. I don't know that you did, I  
11 just simply understood it that way. This that we  
12 see on page 124 of Exhibit 313 isn't a transcription  
13 of Dr. Miller's view, I take it.

14 A. I really don't know that.  
15 I think he may have written this in at the time that  
16 we were in our final session, but I can certainly  
17 find that out for you, that is no problem, if you  
18 wish that information I will get it for you.

19 MR.ROLAND: Thank you, Doctor, those  
20 are my questions.

21 THE COMMISSIONER: Yes, Ms. Chown.

22 CROSS-EXAMINATION BY MS. CHOWN:

23 Q. Dr. Mirkin, my name is Chown  
24 and I appear here on behalf of a number of the  
25 doctors at the Hospital for Sick Children. I want  
to follow up very briefly on a couple of areas that





1  
2 Mr. Roland and some of the other counsel have touched  
3 upon.

4 You have indicated to us what material  
5 your team reviewed with respect to this child, and  
6 I understand that consisted of the child's  
7 medical record, the Zebra pack and any other informa-  
8 tion of that nature that was available to you.

9 I further understood you to say in  
10 that material your team was focussing its attention  
11 particularly on what symptoms were evident in the  
12 material to indicate digoxin toxicity, and you  
13 referred to nausea as one example of that; any  
14 rhythm disturbances; and any other physical  
15 findings that might be relevant such as changes in  
16 the liver. You have also told us that you relied  
17 on serum levels. Have I fairly summarized the basis  
18 of your study as far as the material went?

19 A. That is correct.

20 Q. Would I be fair in saying that  
21 in effect what your team was doing was quite similar  
22 to what a clinician with the day to day responsibility  
23 for each of these patients would be doing in the  
24 management of the digoxin treatment of the  
25 patient.

A. Well, I think with the obvious





1  
2 advantage that the clinician would be able to see the  
3 patient and make judgments that we could only infer  
4 at. So I think the clinician would be in a far  
5 superior position probably to make subtle interpreta-  
6 tions of nuances that we can only infer at.

7 Q. But as far as the process itself  
8 goes, as I understand it, a clinician would look at  
9 the child and make certain observations, looking for  
10 such symptoms as nausea, rhythm disturbances, examining  
11 serum levels and determining whether the child was  
12 showing symptoms of digoxin intoxication; you were  
13 reduced to simply looking at the material and not  
14 the child itself, the review process was similar in  
15 that regard.

16 A. I think that is fair.

17 Q. You told Ms. Forster earlier  
18 that you yourself were not surprised in reviewing this  
19 group of 36 patients to see some patients showing  
20 indications of digoxin intoxication.

21 A. That is correct.

22 Q. Would it be fair to say that  
23 this is a drug that requires careful management in  
24 patients because of the varying individual  
25 responses to the drug?

A. Certainly.





1  
2 Q. Would it be fair also to  
3 say that one of the difficulties in management of the  
4 drug is that the symptoms which may be indicative  
5 of digoxin intoxication are non-specific in that they  
6 may also be indications of other problems in the  
7 child.

8 A. Well, I guess it depends on  
9 what you mean by non-specific.

10 Q. Can I use the example then of  
11 nausea, that is something that may be indicative of  
12 digoxin intoxication, but my understanding is that  
13 nausea is a relatively common occurrence in small  
14 children, especially those who are suffering from  
15 some sort of other illness.

16 A. Well, I don't know how common  
17 nausea is. In fact, I don't think the term nausea  
18 would be appropriate to use here. I think emesis,  
19 we don't know when a baby is nauseous, do we?  
20 I only know when a patient is nauseous when that  
21 person tells me.

22 Q. A baby can't do that so you  
23 are reduced to really actual physical manifestations  
24 of it, then.

25 A. Yes. So I think emesis --

Q. Emesis --





1  
2 THE COMMISSIONER: Emesis, I am sorry,  
3 is that vomiting?

4 THE WITNESS: Correct, regurgitation.  
5 Now, if one were to get me to talk about the  
6 frequency with which emesis occurs, I probably would  
7 have to plead ignorance on knowing how frequent  
8 an event that is. So I don't want to split hairs  
9 with you, I realize I may be doing this, I do want  
10 to get to the non-specific nature of this, but is  
11 it non-specific. But is it really non-specific?  
12 The nausea will occur when an individual has  
13 gastrointestinal disease, gastroenteritis,  
14 and I am not sure how can -- now, that is one system,  
15 one disease state, I call it. Most infants in a new-  
16 born nursery probably don't exhibit emesis. Emesis  
17 is something that probably might be seen in patients,  
18 perhaps with congenital heart disease, I think this  
19 is not uncommon certainly and let us say with  
20 digitalis intoxication. So in that sense emesis  
21 might occur as a consequence of the disease and/or  
22 as a consequence of the drug treatment, so in that  
23 context I think I say yes to you.

24 Q. Doctor, we have been using  
25 the phraseology throughout the inquiry to say that  
certain things might plug into the word emesis;





1  
2 certain things are consistent with digoxin toxicity,  
3 but perhaps not necessarily indicative of digoxin  
4 toxicity, would you be content with that kind of  
5 expression with respect to this symptom?

6 A. Certainly.

7 Q. Similarly, with such things  
8 as rhythm disturbances, I believe several times  
9 in your testimony you have stated, and indeed that  
10 is reflected in your group's report that it is  
11 difficult, I think this morning you used the word  
12 judgment call, to attribute whether rhythm disturbances  
13 are related to digoxin intoxication in an  
14 individual, or to the individual's underlying anatomical  
15 problems.

16 A. Yes, I think that's correct.

17 Q. Again, using the earlier  
18 language, rhythm disturbances might then be described  
19 as something that may be consistent with digoxin  
20 intoxication but not necessarily indicative of it.

21 A. Well, of course, there are  
22 some anatomical disorders, or abnormalities I would  
23 say, which predispose less commonly to arrhythmias  
24 than others. So we must put a bit of a qualification  
25 on that.

Q. I appreciate that, but speaking





1  
2 in general terms, if a child had the kind of  
3 anatomical problem that would predispose that child  
4 to rhythm disturbances, one might then find one's  
5 self in the difficult area of determining causation  
6 of the rhythm disturbances if the child was also on  
7 digoxin.

8 A. I think that could occur, too,  
9 certainly.

10 Q. Doctor, in the clinical setting  
11 the physician then as we have said is charged with  
12 deciding what the appropriate maintenance dose for  
13 a child on digoxin should be. I understand it is  
14 the general practice to start the child on a conserva-  
15 tive maintenance dose and then to observe the child's  
16 response to that dose and then to make any adjust-  
17 ments in the dose based on those observations.  
18 I further understand that the general procedure  
19 as practiced at the Hospital for Sick Children is  
20 when the doctors become aware of symptoms that  
21 might be related to digoxin toxicity, it is the  
22 general practice to hold the digoxin and order  
23 a digoxin level; following the receipt of that  
24 level and combined with the clinical view of the  
25 child to either stop the dosage or adjust it generally  
downwards, but presumably upwards as well if necessary.





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2 In your experience is that an appropriate way to  
3 deal with the administration and adjustment of  
4 digoxin in the management of the patient?

5 A. Yes. I think the management  
6 plan at your institution are consistent with  
7 the accepted medical practice in North America,  
8 if not Canada.

9 Q. We are still part of North  
10 America. Can you confirm, Dr. Mirkin, that when  
11 you were reviewing the material on each child that  
12 you reviewed the dosages that were ordered for  
each child with respect to digoxin.

13 A. We did and I can tell you  
14 in response to the next question that they were all,  
15 in our opinion, within acceptable therapeutic  
16 range.

17 Q. I would like to take you  
18 very briefly to a couple of the individual  
19 patients and simply talk about the management of  
20 the drug by the physicians. The first child I  
21 would like to refer to is Richard McKeil found at  
22 page 89 of your report, Exhibit 313.  
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A. I'm sorry, I am just a bit behind you. Oh, yes, that is No. 10. Go ahead please.

Q. And in Richard McKiel, as several other counsel indicated, there was a high level of digoxin found on October 14th and the response of the doctors to that was to hold the digoxin. The child died the following day on October 15th. The level reported was 4.7 I believe. In your view, was that an appropriate immediate response on behalf of the physicians to a reported level of 4.7?

A. Yes, I think this was appropriate.

Q. The next child I would like to refer you to is Real Gosselin and it is found at page 49 of Exhibit 313; it is your Code No. 29.

Doctor, this is the child that was transferred to The Hospital for Sick Children from a hospital in Winnipeg and he had been digitalized at the prior hospital and was found on admission to have a digoxin level of 3.9. The physician's response on learning of that level was to order the digoxin held. Would you consider that an appropriate response to that level?





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A. Correct, that was an  
appropriate response.

4 Q. And that child was only in  
the hospital one day, so there was no further  
response after that, after the child's death.

6 Similarly in the case of Janice  
7 Estrella, which is found at page 26 of Exhibit 313  
8 and is your Code No. 21, there is some difficulty  
9 in managing her levels.

10 THE COMMISSIONER: I'm sorry, have  
11 you found it?

12 MS. CHOWN: Page 25 on Exhibit 313.

13 Q. Some difficulty in managing  
14 her levels and you have noted in your review of the  
15 chart after a level of greater than 5.0 that was  
16 found on January 7th the doctors ordered her dose  
17 held and thereafter the levels appear to come down.  
18 Did you consider that an appropriate response to that  
reported level?

19 A. Yes.

20 Q. And a similar situation takes  
21 place with Kevin Pacsai who is found at page 110 of  
22 Exhibit 313 and was referred to by Mr. Roland simply  
23 that after a high level of digoxin was noted the  
24 physicians ordered no further digoxin administered  
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until the child's death.

Would you consider that an appropriate response on the part of the doctors?

A. Correct, I would.

Q. And with respect to making adjustments in the doses I think the case of Frank Fazio, which is found at page 30 of Exhibit 313 and is your Case No. 22 -- I'm sorry, page 29, is appropriate to look at there my review of Frank Fazio's medical record shows a few more serum levels recorded than you have recorded at page 30 of Exhibit 313. But it appears that on January 7th there was a serum level of 1.6 obtained, on January 12th a serum level of 1.8, on January 13th a serum level of 1.7. During that time, as you have noted, there were some changes made in the daily dosage to be administered IV with the total daily dosage dropping from 20 to 14 to 10.

Given those readings, would you consider that an appropriate reduction in dosage?

A. Yes, I think that was very good since it did keep subsequent blood levels in a reasonable range.

Q. Yes. And that is reflected in a level at January 26th of 1.5. So, the level has





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come down.

Thank you, Doctor, those are my questions.

THE COMMISSIONER: All right. I think Mr. Young indicated he was not going to ask any questions, is that right? I think so, he is not here.

Ms. McIntyre?

MS. MCINTYRE: Yes, I believe that is right, so, I guess that makes me next.

THE COMMISSIONER: Yes. Now, the only thing I still am eyeing the Court of Appeal but I won't start getting restless until about five to four. You would like to proceed now?

MS. MCINTYRE: Well, I can start.

THE COMMISSIONER: Well, you start now and if you don't finish but around about ten or five to four I may interrupt you and just leave.

MS. MCINTYRE: Certainly.

THE COMMISSIONER: And I will say again you can have perfect liberty to carry on but I won't be here.

I think I would like, and I am quite sure that Dr. Mirkin is even keener than I am, to finish him tomorrow. Is there anyone who contemplates





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that he might have any difficulty in coming in at ten o'clock tomorrow morning because I am quite willing to come in at 9:30. That doesn't disturb you, does it, 9:30 tomorrow morning?

THE WITNESS: How could I say no to you?

THE COMMISSIONER: Okay, it's been done. Well, is there a problem? Does anybody foresee a problem that we need to get here at 9:30? Well then, all right. Well then, you carry on, Ms. McIntyre. You don't plan to be much more than a half hour, do you?

MS. MCINTYRE: No, I don't think I will. Do I take it we are coming at the usual hour then?

THE COMMISSIONER: At ten o'clock then, yes.

MS. MCINTYRE: Okay. Thank you.

CROSS-EXAMINATION BY MS. MCINTYRE:

Q. Dr. Mirkin, I am Elizabeth McIntyre, I am here on behalf of the Registered Nursing Association of Ontario and various nurses at the Hospital.

First, I would like to ask you about electrocardiograms generally. You have referred





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to them frequently in your evidence. I take it that you feel that they are an important tool in assessing digoxin intoxication?

A. I think they help in identifying the presence or absence of arrhythmias, disturbances in the rhythm of the heart. They also provide some insight as to whether or not digitalis is actually being given to the patient by changes in configuration of the electrocardiogram. So, the answer is, yes.





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Q. Do I take it that there are specific indicators on the electrocardiogram that do indicate that digoxin is being given?

A. I don't think one could go that far. There are no so-called pathognomonic features of the electrocardiogram.

Q. I am not sure I understand what that word means.

A. I am going to get on to it, I'm sorry.

Q. Okay, thank you.

A. There are no characteristics of the electrocardiogram that I would say are categorically and only associated with digitalis intoxication. There are characteristics of the electrocardiogram that can be found following administration of other drugs that may be similar to those occurring in digitalis intoxication.

Q. So, the indicators are not specific to digoxin intoxication?

A. Correct.

Q. Are there indicators that are different from detecting that digoxin is given on the one hand to detection of digoxin intoxication on the other hand?





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A. I think that that is probably -- one could say yes to that, that the so-called discernment of whether digitalis has been administered can be determined or inferred by changes in specific segments of the electrocardiogram. One can say, as you have heard many times, there is a dig. effect and the dig. effect is characteristic of someone receiving digitalis and probably would not be observed with any other common agent that I can think of right now.

Now, to distinguish from this first circumstance, dig. effect, which essentially confirms in some way that digitalis has been given or is being given chronically is the detection of digitalis intoxication.

Now, with digitalis intoxication, as you know, there are many changes in the electrical rhythm and configuration of the electrocardiogram. These include I think every abnormality that has ever been described in the literature.

Q. Would that also include the dig. effect that you have referred to?

A. If the dig. effect, so to speak, was not obscured by the total disarrangement of the electrocardiogram, one would also probably see





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EE2.32 that so-called dig. effect which is a change in the  
3 ST segment of the EKG.

4 Q. Well, let me tell you what  
5 I am getting at. A number of these children were  
6 on monitors.

7 A. Monitors?

8 Q. Yes, on monitors at the  
9 time of their death. What I am wondering, if they  
10 were given digoxin or given an overdose of digoxin,  
11 would that have been -- is that something that could  
12 have been picked up on the monitor?

13 A. I think again I will  
14 qualify this with the statement that I am not an  
15 expert in intensive care neonatal medicine, you  
16 must understand that, but if this is a monitor that  
17 essentially is playing out the electrocardiogram -  
18 is that correct?

19 Q. That is what I understand.

20 A. Yes.

21 Q. It is not necessarily  
22 printing it out unless requested to do so.

23 A. Yes, it is on an oscilloscope.

24 Q. Yes.

25 A. A TV screen.

Q. Yes.





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A. The oscilloscope displays essentially what is printed on an electrocardiogram. So, if one looks at that with a modest degree of experience, in my opinion one can see the dig. effect, one can see changes in rhythm that might in a sense alert the observer to the fact that digitalis is doing something.

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Q. And that should include all the pediatric cardiologists that would be working on the unit, would it not?

A. Well, I would assume they are certainly experts and they would be able to discern that, I believe.

Q. Okay. Thank you.

Mr. Commissioner, I have a series of questions on Baby Inwood and I think perhaps it might take me more than five minutes. So, perhaps we should break at this point.

THE COMMISSIONER: Well, you see, if we start at 9:30 if you are snappy and prompt we will perhaps get through it even before 4:30 tomorrow night, that's always a possibility.

MS. MCINTYRE: I am certainly willing to be here at 9:30.

THE COMMISSIONER: All right. Well, then, let's meet at 9:30. Is there any problem? Well, it doesn't matter, you will keep us occupied until 10, I am sure, will you not, if you work on it you might be able to.

MS. MCINTYRE: Probably by tomorrow morning, yes.

THE COMMISSIONER: Yes, all right.





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Is there any problem?

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MR. LAMEK: No, no problem.

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THE COMMISSIONER: All right. Well,  
then, until 9:30 tomorrow morning. I took you  
original agreement to be still valid.

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THE WITNESS: Oh, yes. I didn't know  
it had a retrospective quality to it.

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--- whereupon the hearing adjourned at 3:45 p.m. to  
resume on Wednesday, January 12, 1984 at 9:30 a.m.

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